University of North Carolina at Chapel Hill
Consent to Participate in a Research Study
Adult Participants

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IRB Study #: 21-2224
Title of Study: Dynamic neural mechanisms of brexanolone-induced antidepressant effects in postpartum depression
Principal Investigator: Susan Girdler, Ph.D.
Principal Investigator Department: School of Medicine, Psychiatry
Principal Investigator Phone number: (919) 623-4469
Principal Investigator Email Address: susan_girlder@med.unc.edu
Co-Investigators: David Rubinow, MD; Samantha Meltzer-Brody, MD; Riah Patterson, MD; Flavio Frohlich, PhD; Justin Riddle, PhD; Alana Campbell, PhD; Elizabeth Andersen, PhD; Kai Xia, PhD (Department of Psychiatry)

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Study Contact: Rachel Kozik
Study Contact Telephone Number: (860) 573-4308
Study Contact Email: Rachel_kozik@med.unc.edu

CONCISE SUMMARY

The purpose of this study is to determine the feasibility of performing multiple electroencephalographic (EEG) recordings, semi-structured interviews, and frequent mood assessments on women with postpartum depression (PPD) who are receiving inpatient brexanolone treatment. The information we learn by doing this study may help us develop novel methods for assessing changes in mood associated with brexanolone treatment in women with moderate to severe PPD.

Participants in this study will undergo medical screening to determine if they are eligible to receive brexanolone treatment and complete the research protocols described in more detail in this form. If eligible, participants will be admitted to the N.C. Women's Hospital on the campus of UNC-Chapel Hill for four days. During this inpatient stay, participants will receive 60 hours of brexanolone infusion treatment while also completing 5 research visits involving EEG recordings, measurements of heart rate variability, interviews, and questionnaire surveys about mood state and symptoms. Participants will be asked to complete a virtual follow-up visit approximately 30 days after their brexanolone infusion, during which they will complete electronic surveys about their mood, stress, and symptoms, and provide feedback to the study team during an exit interview.

Due to the necessary inpatient hospital stay, **participants must be fully vaccinated against COVID-19 and provide documented proof of vaccination** prior to enrolling in this research study.

The brexanolone treatment can cause serious side effects, including excessive sedation and loss of consciousness. Because this could cause serious harm, a medical professional will monitor participants for symptoms of excessive sleepiness every 2 hours while they are awake. Other less serious, but common side effects include dry mouth and flushing of the skin or face. There are no medical risks associated with the EEG recordings, but there may be slight discomfort while the EEG cap is placed on the scalp, including scalp irritation, headaches, and disturbance of hair aesthetics. There may be some discomfort, pain, or bruising associated with phlebotomy. The device used to measure heart rate variability will be adhered to the participant's torso using gel electrodes. There may be some skin irritation or discomfort associated with adhering or removing these electrodes. Items in the interview and surveys are designed to assess lifetime psychiatric symptoms and mood disturbances and may be associated with some psychological distress.

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

What are some general things you should know about research studies?

You are being asked to take part in a research study. To join the study is voluntary.

You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies.

Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

The purpose of this research study is to collect preliminary data on the ways in which ZULRESSO® (brexanolone) affects electrical brain activity in adult women who have been diagnosed with postpartum depression (PPD).

On March 19, 2019, brexanolone was approved by the US Food and Drug Administration (FDA) under the name ZULRESSO for the treatment of PPD in adults. Brexanolone infusion is a rapidly acting intravenous therapy and is the first treatment approved by the FDA for PPD. This study seeks to collect data on the brain mechanisms that underly the antidepressant effects of brexanolone in women with PPD. In doing so, we will evaluate the feasibility of collecting five (5) electroencephalographic (EEG) recordings, along with other measures of mood and PPD symptoms, over the course of the 60-hour infusion of brexanolone.

In this study, you will receive brexanolone during the treatment period. You will receive the study drug (brexanolone) by intravenous (IV) infusion (by a needle attached to a bag, inserted into a vein in your arm). It will be given in addition to other medications you may already be taking. You will receive all other medications and treatment as per standard of medical care and as deemed appropriate by the study doctor. This study involves staying overnight at the clinic for up to four nights.

Because this is a research study, brexanolone will be given to you only during the study and not after the study is over.

You are being asked to take part in this research study because you are between the ages of 18 and 45 and are within nine months postpartum. You meet diagnostic criteria for moderate or severe postpartum depression with onset during the third trimester of pregnancy or within four weeks of delivery. You are not currently breastfeeding, or you are willing to temporarily stop breastfeeding for seven days (including the 4 days of infusion and 3 days after). You are on a stable regimen of any current psychotropic drugs (those that affect mental state) for at least 28 days prior to enrollment and have been on a stable dosage for at least 14 days prior to enrollment. You are also on a documented form of contraception to prevent pregnancy while you are enrolled in this study (from screening period through follow-up visit). You have been fully vaccinated against the COVID-19 virus and can provide documented proof of vaccination. You have provided signed informed consent and agree to adhere to all study requirements.

Are there any reasons you should not be in this study?

You should not be in this study if you meet one or more of the following criteria:

- You are currently pregnant or breastfeeding
- Your most recent pregnancy resulted in a stillbirth, termination, or a child that was placed for adoption
- You have kidney impairment or failure, liver impairment or failure, or anemia
- You have an untreated or inadequately treated thyroid disorder
- You have a known allergy to progesterone or allopregnanolone
- You had a suicide attempt during this episode
- You have a history of bipolar disorder, schizophrenia and/or schizoaffective disorder
- You have current psychotic symptoms including delusions, hallucination, or a formal thought disorder
- You have current alcohol or substance use disorder
- You have received electroconvulsive therapy (ECT) during this episode

- You have a history of seizure disorder
- You are currently taking benzodiazepines or anticonvulsant agents
- You have had exposure to an investigational medication or device within 30 days
- You have previously participated in any study using brexanolone or SAGE-217
- You are an investigative site personnel, sponsor personnel, or an immediate member of their family
- You have not been fully vaccinated (with documented proof) against the COVID-19 virus.

How many people will take part in this study?

This study is being carried out at the University of North Carolina (UNC) at Chapel Hill, specifically UNC Hospitals, and will enroll approximately 10 women.

How long will your part in this study last?

Participation in this study will last up to 7 weeks and will include the following visits:

- Screening Period: This visit will occur within fourteen (14) days of signing this consent form. This visit may take up to 4 hours. Portions of this screening period may be conducted virtually, over secure, HIPAA-compliant web-based video platform (i.e., Zoom). Other portions of the screening process must be completed in-person, at a clinic on the campus of UNC Chapel Hill.
- Treatment Period: This will involve staying overnight in N.C. Women's Hospital for four nights, will consist of a 2.5-day (60 hour) infusion of brexanolone and assessments 12 hours after the infusion has been stopped.
- Follow-up Period: This will involve 1 visit approximately 30 days after the start of the infusion. This visit may take up to 2 hours and can occur either in-person, over the phone, or over secure, HIPAA-compliant web-based video platform (i.e., Zoom)

What will happen if you take part in the study?

The Screening Period:

Before any study-related tests and procedures are performed, we will ask you to read and sign this consent form. The following tests and procedures will be performed to determine if you qualify to take part in this study:

- **You must be fully vaccinated against the COVID-19 virus and provide documented proof of vaccination. You will be required to provide proof of vaccination prior to attending in-person study visits.**
- Review your medical history and your psychiatric history.
- Collect personal details about you including age, race, and ethnicity.

- Review any medications you are currently taking, have taken recently, and any type of therapy you have participated in to treat your current postpartum episode.
    - You may continue taking medications that affect your mood while you are on the study, as long as you started the medication at least 28 days prior to enrollment. You will not be able to change doses or begin new medications during the screening period and until at least 72 hours after the start of the study drug infusion.
    - You can't have received electroconvulsive therapy (electrical stimulus of the brain) to treat your current episode of PPD.
- Physical examination
- Measure your vital signs (temperature, breath rate, heart rate, blood pressure, height, and weight).
- A test to measure the electrical activity of your heart, called an electrocardiogram (ECG).
- Collect blood samples for:
    - Standard safety laboratory tests including:
        - Hematology: CBC (red blood cells, white blood cells with differentiation and absolute values, hemoglobin, hematocrit, reticulocytes, and platelets)
        - Coagulation: activated partial thromboplastin time, prothrombin time, and international normalized ratio
        - Biochemistry: serum electrolytes (sodium, potassium, chloride, bicarbonate or total carbon dioxide, calcium, and phosphorus); renal function tests (creatinine and blood urea nitrogen); liver function tests (total bilirubin, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, and gamma glutamyl transferase); thyroid stimulating hormone; total protein; albumin and glucose
    - A pregnancy test. The results of the test must be negative for you to take part in the study.
    - A total of 20.1mL of blood will be drawn at this screening visit, which is approximately 1.4 tablespoons
- Collect urine sample for:
    - Alcohol screening. The result of the alcohol screen must be negative for alcohol for you to take part in the study.
    - Drug Screening. The result of the drug screening must be negative or explained by a prescription medication you may be taking for you to take part in the study. Medical marijuana is not allowed.
- You will be asked questions about your psychiatric symptoms, including depression symptoms, your feelings and emotions, as well as any thoughts about suicide. You will also be asked questions about your pregnancy history, and experiences with symptoms of postpartum depression. You may choose to not answer a question for any reason.

The study doctor will use the information noted above and other recent information in your medical records to determine if you are able to take part in the study. We will ask you to sign a separate authorization for release of your personal medical records to the study personnel listed

on this consent form. There may be reasons why you are not able to take part, and the study doctor will discuss those with you.

The entire screening period will last approximately 4 hours. Most of the items listed above must be completed in person, at a clinic on the campus of UNC Chapel Hill. However, you may choose to complete portions of the screening period virtually (i.e., over Zoom), rather than during your in-person screening visit. The portions that may be completed virtually can include: the psychiatric screening, collection of demographic information, and review of medical and pregnancy history. The optional virtual session will take approximately 2 hours. Therefore, if you decide to complete this portion virtually, then the in-person visit will take 2 hours, and the virtual portion will take another 2 hours. If you agree to participate in this research study, then you will be required to complete all the screening protocols listed above. You will have to option to complete everything in-person, or a combination of in-person and virtual appointments.

1. The Baseline Visit

(Day 1, Hour 0)

If you agree to take part and the study doctor determines you can take part in this study, you will be admitted to UNC Hospitals to begin participation in the treatment period of this research study protocol. Prior to administration of the brexanolone infusion, you will complete a baseline study visit.

Baseline Procedures (Hour 0):

EEG: You will be fitted with an EEG cap (much like a swimming cap) with 128 electrodes placed on your head to record your brain activity. It will be necessary to apply gel to your scalp so that the electrodes can obtain a better electrical signal. Once the EEG cap is placed, you will be asked to rest quietly for 8 minutes, alternating your eyes open and closed while the electrodes record your brain activity. The EEG cap will remain on your head for the first day of the treatment period (hours 0 through 8). Cap set up will take approximately 30 minutes and the first recording will last 8 minutes. After this first recording, the cap will remain in place for the rest of the day, until you complete the recording at Hour 8. Although the cap will stay on your head during the first day, it will only be recording your brain activity for the 8-minute sessions of rest described at Hours 0, 4, and 8.

Heart Rate Variability: Heart rate data will be recorded using a chest-mounted device, the FAROS 180. This will attach to your torse using two disposable electrodes, one placed near your collarbone and the other placed on your lower ribcage. The FAROS 180 is a Class II medical device and is designated for research use. The device will record your heart rate the entire time it is adhered to your skin. You will be asked to place the device on your skin at Hour 0 and leave it on your skin for the duration of the time you are hospitalized (through Hour 72).

Interview Recording: You will also be asked to complete a verbal interview with study investigators to assess symptoms of depression. You will be asked to respond to a series of standardized questions verbally while a laptop camera records your facial expressions. The video recording of this interview will last approximately 10 minutes. Following the interview, you will

be asked to recall two events from your life and to concentrate on those memories for 60 seconds while a laptop camera records your facial expressions. You will not be asked to share details of these life events with the research team, but only to contemplate these events silently during the video recording. You will be asked to rate your emotional experience while you contemplated those life events. Researchers will also ask you to come up with a word or phrase that will help you to remember each of the two life events. At later sessions, the research team will repeat those words or phrases back to you in order to cue your memory of these life events for later video recordings. The recordings will be saved on a secure, password protective drive and used for later analysis of nonverbal facial expression. Only research personnel listed on this consent form will have access to these recordings.

Surveys: You will be asked to complete a series of electronic questionnaires that will assess your mood, symptoms of PPD, and emotional state. You do not have to answer any questions that you do not wish to answer.

2. The Treatment Period:

Days 1-4 (Hours 0-72)

IV Infusion (Hours 0-60)

Following the baseline procedures outlined above (EEG recording, interview recording, and questionnaires), you will be started on a continuous IV infusion of brexanolone.

The study staff will use a needle to insert a small hollow tube into a vein in your hand or arm.

The needle is removed, but the tube temporarily remains in your hand or arm to get the study drug into your body. The tube will be cleaned with a small amount of saline (salt water) before and after it is used.

In total, you will continuously receive brexanolone for 60 hours, which will span 3 calendar days (Days 1–3). The IV infusion will be stopped and the tube removed at the end of Day 3.

In addition to the continuous IV infusion, the following tasks will occur at the indicated timepoints during the treatment period of this study:

Hour 4 (Day 1):

EEG: You will be asked to complete a second EEG recording, following the same procedures as outlined above. The EEG cap will remain on your head after this session.

Interview Recording: You will also be asked to complete a second interview with study investigators and your responses will be video recorded so that investigators can analyze your nonverbal facial expressions. You will be asked to recall the two life events that you thought about from your first interview recording and the research team will recite the word or phrase that you came up with to help cue you to these memories. You will be asked to think of these same memories again for 60 seconds while the laptop camera records your facial expressions.

Then you will be asked to rate your emotional experience of recalling these memories. This will follow the same procedures as outlined above.

Surveys: You will again complete a series of electronic questionnaires to assess your mood, symptoms, and emotional state.

Hour 8 (Day 1):

EEG: You will be asked to complete a third EEG recording, following the same procedures as outlined above. At the end of this recording, the EEG cap will be removed.

Interview Recording: You will also be asked to complete a third interview with study investigators and your responses will be video recorded so that investigators can analyze your nonverbal facial expressions. You will be asked to recall the two life events that you thought about from your first interview recording and the research team will recite the word or phrase that you came up with to help cue you to these memories. You will be asked to think of these same memories again for 60 seconds while the laptop camera records your facial expressions. Then you will be asked to rate your emotional experience of recalling these memories. This will follow the same procedures as outlined above. This will follow the same procedures as outlined above.

Surveys: You will again complete a series of electronic questionnaires to assess your mood, symptoms, and emotional state.

Hour 28 (Day 2):

EEG: The EEG cap will be set up again, following the procedures outlined at Hour 0. You will be asked to complete a fourth EEG recording, following the same procedures as previous EEG sessions.

Interview Recording: You will also be asked to complete a fourth interview with study investigators and your responses will be video recorded so that investigators can analyze your nonverbal facial expressions. You will be asked to recall the two life events that you thought about from your first interview recording and the research team will recite the word or phrase that you came up with to help cue you to these memories. You will be asked to think of these same memories again for 60 seconds while the laptop camera records your facial expressions. Then you will be asked to rate your emotional experience of recalling these memories. This will follow the same procedures as outlined above. This will follow the same procedures as outlined above.

Surveys: You will again complete a series of electronic questionnaires to assess your mood, symptoms, and emotional state.

Hour 72 (Day 4):

This session will occur 12 hours after the brexanolone infusion has ended, while you are still in the hospital. During this session, we will complete our fifth and final EEG recording, interview recording, memory recall, and survey administration, following the same procedures as the previous four sessions.

Following data collection, you will undergo a series of safety assessments before being discharged from the hospital. These assessments will include the collection of vital signs, blood samples for safety labs and hormone levels, and the assessment of suicidality.

During the treatment period, the following will be completed (**some checks will be done multiple times a day**):

- Review any changes in your health or medications.
- A sensor will be placed on your finger to monitor the oxygen levels in your blood.
- During the infusion, subjects may get extremely sleepy. A study doctor or staff will be available continuously on-site to oversee your treatment for the duration of the infusion. A study doctor or staff will check you for symptoms of extreme sleepiness every 2 hours during times you are not planning to be asleep.
- Measure of your vital signs (temperature, breath rate, heart rate, and blood pressure).
- Collect blood samples for hormone levels on Days 1, 2, and 4. At each collection point, we will collect 5mL of blood (approximately 1 teaspoon).
- You will be asked questions about your depression symptoms, feelings and emotions, your postpartum experience, as well as any thoughts about suicide (Days 1-4). You may choose to not answer a question for any reason.

3. The Follow-up Period:
(Day 30)

Approximately 30 days after the start of your brexanolone infusion, a follow up session will be scheduled. During this session, you will complete a series of survey questionnaires to assess your postpartum and mood symptoms, and your current emotional state. You will also be invited to have an exit interview with the study team, during which you will have the opportunity to share feedback about your experience in the study and answer questions about how you have felt since receiving the drug treatment. This session will last up to one hour and can be completed in-person or over Zoom, whichever is more convenient.

EXPECTATIONS

If you take part in this study, you must:

- **Be fully vaccinated against the COVID-19 virus and provide documented proof of vaccination prior to participation in this research study.**
- Keep all your appointments and follow all instructions given by the study doctor or staff.
- Not take any new medications, herbal medications, supplements, or vitamins after signing this consent form (including over-the-counter, prescription, or illegal) except if the study doctor allows it. Study drug and some medicines may interact with each other and cause

serious side effects. Your study doctor will decide if other medicines can be taken with study drug.

- Tell your study doctor about all your medical conditions, including if you:
  - drink alcohol
  - have kidney or liver problems
  - are pregnant or think you may be pregnant. It is not known if brexanolone will harm your unborn baby.
  - are breastfeeding or plan to breastfeed. Brexanolone passes into breast milk. Talk to your study doctor about the risks and benefits of breastfeeding and about the best way to feed your baby while receiving study drug.
- Especially tell your study doctor if you take:
  - other antidepressants
  - opioids
  - CNS depressants such as benzodiazepines
  - Anti-seizure medications
- Tell the study doctor of any problems or side effects that you have while you are in the study.
- Remain at the study center on Days 1-4 until all study procedures are completed.
- Not drive a car or do other dangerous activities after your study drug infusion until your feeling of sleepiness has completely gone away. You may need to make plans for someone to drive you home from the study site.
- Have a caregiver or someone who will care for your child(ren) and be in the room with you if you are with your child(ren) during the infusion. The study staff will discuss these arrangements with you in more detail.

What are the possible benefits from being in this study?

Research is designed to benefit society by gaining new knowledge. You may or may not benefit from taking part in this study. If brexanolone works for you, your symptoms of postpartum depression may improve while you take part in this study. Results from this study may benefit others in the future.

What are the possible risks or discomforts involved from being in this study?

Brexanolone

- Brexanolone has been studied in 13 clinical studies, which have been completed in the brexanolone PPD clinical program. A total of 367 unique subjects have been exposed to brexanolone across the completed clinical studies in PPD clinical program.
- The safety of brexanolone in PPD is reflected in the experience of 247 subjects with PPD (140 treated with brexanolone and 107 treated with placebo) who participated in three studies of brexanolone conducted in adult subjects with postpartum depression, which are most relevant for your participation in this study. All subjects were 18 years of age or older.
- The summary of the side effects that were seen in the three studies and may have been related to brexanolone is presented below. No subjects died in the brexanolone clinical

program. Most side effects seen in these studies were mild, and in most of the subjects the side effect resolved and the treatment with brexanolone was continued without incident. In some cases, the dose of the brexanolone treatment was lowered and the treatment continued without incident. Some side effects, however, were severe (described below).

Important information:

Brexanolone can cause serious side effects, including:

- Excessive sedation and sudden loss of consciousness: brexanolone may cause you to feel very sleepy (excessive sedation) or pass out (loss of consciousness). This is different from normal sleep where you drift into sleep naturally and can wake up easily. Sudden loss of consciousness (passing out) can occur in some patients.
- Because this could cause serious harm, your study doctor should check you for symptoms of excessive sleepiness **every 2 hours while you are awake**.
- During your infusion, tell you study doctor or staff right away if you feel like you cannot stay awake during the time you are normally awake or if you feel like you are going to pass out. Your study doctor may lower your dose or stop the infusion until your symptoms go away.
- You must have a caregiver or family member with you to help care for your child(ren) during your infusion and to be in the room with you if you are with your child(ren) during the infusion.

It is important to tell your study doctor if you have any of the following symptoms while getting brexanolone:

- Feeling more sleepy than usual (you cannot stay awake when you are trying to stay awake)
- Having a hard time paying attention
- Having trouble following simple instructions
- Feeling lightheaded or dizzy or like you are going to pass out

If you start to feel the symptoms listed above, you should:

- If you are holding a baby, put your baby down
- Sit or lie down
- Tell you study doctor right away

Your study doctor may stop your infusion. During clinical trials, once brexanolone was stopped, patients who passed out woke up after a short time. You and your study doctor will decide whether to continue study drug.

Brexanolone can cause other serious side effects, including:

- **Increased risk of suicidal thoughts or actions.** Brexanolone and other antidepressant medicines may increase suicidal thoughts and actions in some people 24 years of age and younger. Depression or other serious mental illnesses are the most important causes of suicidal thoughts or actions.

How can I watch for and try to prevent suicidal thoughts and actions?

- Pay close attention to any changes, especially sudden changes in mood, behavior, thoughts, or feelings, or if you develop suicidal thoughts or actions.
- Tell your study doctor right away if you have any new or sudden changes in mood, behavior, thoughts, or feelings.
- Keep all follow-up visits with your study doctor as scheduled. Call your study doctor between visits as needed, especially if you have concerns about symptoms.

Tell your study doctor right away if you have any of the following symptoms, especially if they are new, worse, or worry you:

- attempts to commit suicide
- thoughts about suicide or dying
- new or worse depression
- other unusual changes in behavior or mood

If you have thoughts of harming yourself, you should go to the nearest emergency department (ED) or call 911. You can also call the National Suicide Prevention Lifeline 24 hours a day at 1-800-273-8255.

The study drug, brexanolone, may have the ability to make someone physically dependent on it.

The following adverse events in PPD clinical program are considered <u>the most common</u> (more than 1 in 20 people and at least twice the rate of placebo) side effects of brexanolone:

- Sedation (drowsiness) /somnolence (sleepiness)
- Dry mouth
- Passing out (loss of consciousness)
- Flushing of the skin or face (flushing/hot flush)

Other side effects which have occurred include:

- Faster than normal heart rate (tachycardia)
- Diarrhea
- Upset stomach (dyspepsia)
- Dizziness, feeling faint (presyncope), feeling of losing the balance (vertigo)
- Mouth and throat pain (oropharyngeal pain)

Treatment with brexanolone may cause the side effects discussed in this section or other side effects that are unknown at this time. The side effects may be minor or could be severe and become life-threatening. The study doctor and study staff will monitor the side effects, and if necessary, your infusion with brexanolone may be stopped.

Study Procedures

- Blood samples: possible side effects from blood drawing include faintness, inflammation of the vein, pain, tenderness, bruising, or bleeding at the site of puncture. There is also a small possibility of infection.
- IV/catheter insertion: possible side effects include discomfort or pain at the site of the catheter placement. There is also a risk of infection, bleeding and/or bruising at the insertion site.
- ECG: skin irritation is rare but could occur during an ECG from the electrodes or gel that is used.
- A temporary intravenous tube flushed with sterile salt water may be placed in a vein in your arm for series of blood samples that are required for the study. The risks include pain, bruising, clotting, bleeding, and possibly infection at the site of the intravenous tube placement. Saline (saltwater solution) or heparin may be used to flush the intravenous tube.
- Questionnaires: completing the questionnaires may make you feel anxious or uncomfortable
- EEG: can cause mild inconveniences including headaches and the disturbance of hair aesthetics.
- Heart Rate Variability: skin irritation may occur at the site where the electrodes are adhered. There may be slight discomfort associated with the removal of these electrodes, especially if they are attached to body hair.

Unforeseen Risks

There may be other risks that are unknown or uncommon which may be severe, could require hospitalization and could become life-threatening.

All drugs have a potential risk of an allergic reaction, which if not treated promptly, could become life-threatening. If you have a very bad allergic reaction, you could die. Some signs that you may be having an allergic reaction are:

- Rash or hives
- Having a hard time breathing
- Wheezing when you breathe
- Sudden change in blood pressure (making you feel dizzy or lightheaded)
- Swelling around the mouth, throat or eyes
- Fast pulse
- Sweating

You should report any problems to the study doctor immediately.

Pregnancy and Birth Control: May I take study drug if I am pregnant?

In order to reduce the risk of pregnancy, you must use an effective method of birth control while you are taking part in this study.

You must use one of the following methods of birth control during participation in this study and for 30 days following the end of the study drug infusion:

- Surgically sterile (either removal of both ovaries or hysterectomy)
- Not engage in sexual relations
- Combined (estrogen and progestogen containing) oral (pills), intravaginal, or transdermal hormonal contraception to prevent ovulation.
- Oral, injectable, or implantable progestogen-only hormonal contraception to prevent ovulation
- An intrauterine device (IUD)
- An intrauterine hormone-releasing system
- Bilateral tubal occlusion (both tubes tied)
- Vasectomized partner

If you are already using a method of birth control, the study doctor or study staff will discuss with you whether your current method of birth control is acceptable for use during this study.

If you become pregnant during the study you should notify the study doctor right away. The study doctor will ask to follow your pregnancy to its outcome.

It is not known if brexanolone will harm your unborn baby. There is a pregnancy registry for females who are exposed to brexanolone during pregnancy. The purpose of the registry is to collect information about the health of females exposed to brexanolone and that of their baby. If you become pregnant during treatment, talk to your healthcare provider about registering with the National Pregnancy Registry for Antidepressants at 1-844-405-6185 or visit https://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/antidepressants/.

Lactation: May I breastfeed my baby if I am taking study drug?

A small study in 12 women indicated that brexanolone is transferred to breastmilk in nursing mothers. However, data show that only 1-2% of the dose received by the mother is transferred to the infant. We do not have data on the impact of brexanolone on milk production or the impact of brexanolone on a breastfed infant. Therefore, in order to participate in this research study, you must temporarily stop breastfeeding for 7 days, including the 4 days of hospitalization and 3 days after.

What should I avoid while receiving study drug infusion:

- Brexanolone may make you feel dizzy and sleepy. Do not drive a car or do other dangerous activities after your infusion until your feeling of sleepiness has completely

gone away. You may need to make plans for someone to drive you home from the facility after brexanolone infusion. See Important information described above
- Do not drink alcohol while receiving brexanolone.

If you choose not to be in the study, what other treatment options do you have?
You do not have to be in this study to receive treatment for your postpartum depression. You may choose to receive in-patient treatment, medications, therapy, or a combination of medications and therapy for your postpartum depression. The study doctor will discuss with you the risks and benefits of the alternative treatments.

What if we learn about new findings or information during the study?
You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

How will information about you be protected?
Personal information about you will be protected in a number of ways including:

- Your name and other identifying information about you will be stored separately from the study data. Your study data will be stored using a code to identify you.
- A linkage file will exist so that the research team can identify you. This file will be kept on secure UNC servers, accessed with a password, only by the members of the research team.

Participants will not be identified in any report or publication about this study. We may use de-identified data and/or specimens from this study in future research without additional consent. Some of your de-identified biospecimens will be analyzed by an outside laboratory. There is a chance your de-identified biospecimens may be used for commercial profit. If this happens, you will not receive any compensation for this work.

Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies (for example, the FDA) for purposes such as quality control or safety.

By signing this informed consent document, you agree that some of the information generated by participating in this study and/or a copy of the consent form may be included in your medical record and that this information may be viewed by other physicians or caregivers who provide healthcare services to you. This will allow the doctors caring for you to know what study medications or tests you may be receiving as a part of the study and know how to take care of you if you have other health problems or needs during the study. Additionally, the information may be shared with your medical insurance plan if the research services provided are billed to your insurance.

Your de-identified study data will also be shared with Sage Therapeutics Inc., who provided a grant to support this research.

Under North Carolina law, researchers are required to report information about the abuse or neglect of a child or disabled adult to local or state authorities.

Under North Carolina law, confidentiality does not extend to certain communicable diseases, such as TB, HIV, hepatitis, or other illnesses that put others at risk. If the researchers become aware that subjects have such an illness, they are required to report it to state authorities.

Audio and Video Recording

Earlier studies suggest that people's mood states change even before they are aware of the change. In this study, it is important for us to detect when your mood state changes as soon as possible. One means of detecting mood states is through analysis of facial expressions. To accomplish the detection of emotion in facial expressions, we will record your face on video for approximately ten minutes while you answer questions about your mood. After the interview questions, you will be asked to think of a sad event from your life and concentrate on that memory for 30 seconds while the laptop camera video records your facial expressions. Then you will be asked to rate your emotional experience of that memory. Next, you will be asked to recall a happy event from your life and concentrate on that memory while the camera records your facial expressions. You <u>will not</u> be asked to share details of these events with the research team. Instead, researchers will ask you to come up with a word or phrase that represents each of the memories, and the research team will recite those words or phrases back to you at later recording sessions to help cue you to the memories you thought about during the first session. The video recording will be performed at baseline and at 4, 8, 28, and 72 hours after the start of the brexanolone infusion. The video recording will be stored on a dedicated laptop computer, which will be stored in a locked file in the investigator's office. Emotion detection will be performed by software analysis of the video recording, which will be erased after the whole study has been completed (approximately two years). The results of the software analysis will be coded (i.e., it will not have any identifying information associated with it), and the code will be stored in a separate, locked file drawer in the investigator's office. You can, at any time, request that the video recording be stopped or not performed. We ask that you give separate consent here for obtaining the video, but you need not give consent to participate in the study AND, as just stated, you can withdraw consent at any time.

Check the line that best matches your choice:

_____ OK to record me during the study

_____ Not OK to record me during the study

Study Communications

The study team would like to message you by text message or email; however you may say "no" to receiving these messages and still participate in this study. If you say "yes," messages may

contain personal information about you and may be sent or received by the study team's personal electronic devices. These messages may be sent in a method that is not able to be encrypted (protected) and there is the risk your information could be shared beyond you and the study team. This information may include information such as reminders and notifications to contact the study team.

If you wish to stop receiving unprotected communication from the study team or have lost access to your device, please notify the study team using the study contact information on the first page of this consent form. After the study is complete and all research activities finished, or you withdraw from the study or request to stop receiving unprotected communication, you will no longer receive un-encrypted (un-protected) messages specific to this study.

_____ Yes, I consent to the study team utilizing the following email address to send communication: _____

_____ Yes, I consent to the study team utilizing the following cell phone number to send communication: _____

_____ No, I do not consent to receive un-protected communication from the study team.

You will be asked to sign a separate form ("HIPAA Authorization") to allow researchers to review your medical records.

What will happen if you are injured by this research?

All research involves a chance that something bad might happen to you. If you are hurt, become sick, or develop a reaction from something that was done as part of this study, the researcher will help you get medical care, but the University of North Carolina at Chapel Hill has not set aside funds to pay you for any such injuries, illnesses or reactions, or for the related medical care. Any costs for medical expenses will be billed to you or your insurance company. You may be responsible for any co-payments and your insurance may not cover the costs of study related injuries.

If you think you have been injured from taking part in this study, call the Principal Investigator at the phone number provided on this consent form. They will let you know what you should do.

By signing this form, you do not give up your right to seek payment or other rights if you are harmed as a result of being in this study.

What if you want to stop before your part in the study is complete?

You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

If you withdraw or are withdrawn from this study all data collected up until the point of

withdrawal will be retained, however no additional information will be collected unless you provide additional written permission for further data collection at the time of your withdrawal.

If you withdraw or are withdrawn from this study before the drug infusion is complete, the infusion will stop, as well. The study team will provide you with referrals and you will be free to seek treatment (including the full course of brexanolone) through traditional routes outside of this research study.

Will you receive anything for being in this study?

You may receive up to $750.00 for taking part in this study. Subjects will be paid $50.00 for the Screening Visit, $100.00 for each of the EEG recordings ($100.00 x 5 = $500.00 total for completion of all EEG sessions), and $200.00 for completion of the Follow Up Visit. You will only be compensated for each study visit completed. You will be paid in the form of a Visa gift card at the end of your participation in this study.

You may be required to complete unscheduled visits to repeat labs, ECG, evaluations, etc. This may be for your safety or the integrity of the trial.

Any payment provided for participation in this study may be subject to applicable tax withholding obligations. Your name, address, and U.S. tax payer identification number (SSN or ITIN) are required to process payments and/or to report taxable income to the IRS. You must complete a W-9 (for U.S. persons) or W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents (for non-resident aliens) in order to receive payment for participation.

U.S. person participants must complete Form W-9 in order to receive payment for participation. If payment by UNC equals or exceeds $600 per calendar year for U.S. persons, UNC will report the amount to the Internal Revenue Service on Form 1099. Nonresident alien participants must complete Form W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents in order to receive payment for participation. Payments to nonresident alien participants may be subject to tax withholding and are generally reported to the Internal Revenue Service on Form 1042-S. This information will not be linked to any of the study data and will only be used for payment purposes.

If you do not provide your SSN or ITIN, or complete the appropriate documentation noted above, we cannot issue you a payment for participation. However, you may still choose to participate in this study.

Will it cost you anything to be in this study?

It will not cost you anything to be in this study.

What if you are a UNC student?

You may choose not to be in the study or to stop being in the study before it is over at any time. This will not affect your class standing or grades at UNC-Chapel Hill. You will not be offered or receive any special consideration if you take part in this research.

What if you are a UNC employee?
Taking part in this research is not a part of your University duties, and refusing will not affect your job. You will not be offered or receive any special job-related consideration if you take part in this research.

Who is sponsoring this study?

This research is funded by Baszucki Brain Research Fund and Sage Therapeutics. This means that the research team is being paid by the sponsor for doing the study. In addition, David Rubinow, a co- investigator on this study, receives money from Sage Therapeutics for work that is not part of this study. These activities may include consulting, service on committees or boards, giving speeches, or writing reports. In addition, David Rubinow holds stock in Sage Therapeutics and has the potential to receive financial benefits in the future.

If you would like more information, please ask the researchers listed in the first page of this form.

What if you have questions about this study?
You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

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

What if you have questions about your rights as a research participant?
All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____
Signature of Research Participant

_____
Date

_____
Printed Name of Research Participant

_____
Signature of Research Team Member Obtaining Consent

_____
Date

_____
Printed Name of Research Team Member Obtaining Consent