A PHASE 1 RANDOMIZED SINGLE ORAL DOSE CROSS-OVER STUDY INVESTIGATING DESMETRAMADOL DOSE PROPORTIONALITY AND FOOD EFFECT IN NORMAL HUMAN SUBJECTS

Syntrix Informed Consent OMNI-PAIN-103

Version: 29 JUL 2020

ClinicalTrials.gov NCT #: 04683926

INFORMED CONSENT FORM

Sponsor: **Syntrix Biosystems, Inc.**

Study Title: **A Phase 1 Randomized Single Oral Dose Cross-Over Study Investigating Desmetramadol Dose Proportionality and Food Effect in Normal Human Subjects**

Study Doctor: **Robert Schwab, M.D.**

Telephone: **(402) 476-2811 (Normal Business Hours)**
(855) 669-7638 (Questions PRIOR to 1st Study Check In)
(402) 613-5822 (24-hour Nurses' Line AFTER 1st Study Check In)

Address: **Celerion**
621 Rose Street
Lincoln, NE 68502

It is important that you give a true and complete medical history. You must be honest about your past and present usage of medications. Giving information that is not true could be very harmful to your health. If you give false information, you may be dismissed from the study.

You are being asked to take part in a research study sponsored by Syntrix Biosystems, Inc. Celerion is being paid by Syntrix to conduct this study. You should read this form before you decide if you want to take part in the study. This form will tell you about the study. The Study Doctor or study staff can explain words or information that you do not understand. Ask the study staff as many questions as needed for you to decide if you want to take part in the study. Research studies are voluntary and include only those who wish to take part. If you decide to take part in this study, you must sign your name at the end of the form and date it. You cannot take part in this study until you sign and date this form.

1. PURPOSE OF THE STUDY

The study drug, desmetramadol, is experimental. That means the United States Food and Drug Administration (FDA) has not approved it for sale or use. Desmetramadol is being studied to treat acute and chronic pain.

An investigational study drug is a drug that has not been approved by the Food and Drug Administration (FDA) and Other Regulatory Agencies but may be used in research studies like this one.

The purposes of this study are to:

- To determine in fasted healthy subjects if following an oral single-dose of 10, 20 and 30 mg of desmetramadol, if the blood levels increase as expected.

- To determine the food effect on 30 mg desmetramadol in healthy subjects following oral single-dose.

- To determine the safety and tolerability of desmetramadol following oral single-dose with or without food.

- Determine pharmacokinetic (PK) parameters for each M5 enantiomer in blood following oral single-dose administration of 10, 20 and 30 mg desmetramadol in fasted healthy subjects and of 30 mg desmetramadol administered with food.

- Quantify total M1 and M5 excreted (unconjugated and de-conjungated) in the urine after the 30 mg fasted dosings and compute clearance of each and in relation to 24 hour creatinine clearance.

2. SUBJECT RESPONSIBILITIES

You must:

- Follow all clinic rules and instructions of the study staff.
- Follow the study restrictions.
- Report any side effects.
- Give true and complete answers to any questions.
- Comply with the terms of the Informed Consent Form.

3. NUMBER OF SUBJECTS AND LENGTH OF STUDY

This study will enroll up to 32 subjects. The entire study will last about 12 days plus up to 31 days for screening. There is 1 confinement period where you will stay in the clinic the entire time. The confinement period will last about 12 days.

4. SCREENING VISIT

The following procedures will be done during this visit(s) to help the Study Doctor determine if you qualify for this study. This is called the screening visit. Screening may consist of 1 or more visits and involves the following procedures.

- Read, sign, and date the Informed Consent Form.
- Provide your medical history including all medications, vitamins, herbal products or supplements you are taking.
- Provide information such as your name, age, date of birth, sex, race, ethnicity, address, social security number or tax identification number, and phone number.
- An ECG - electrocardiogram (a test that measures and records the electrical activity of your heart) will be done.
- A physical examination will be done.
- Height and weight will be measured.
- Vital Signs (blood pressure, pulse rate, respiratory rate, and body temperature, obtained by mouth) will be done.
- Blood and urine samples will be collected. Your blood and urine sample will be used for routine laboratory tests. Your urine sample will be tested for drugs of

abuse and alcohol. If you are female, your blood will be used for a pregnancy test.

- Your blood will also be used to test for HIV and hepatitis B and C. If your results are positive, the laws require that your name and positive result be reported to the local health department. Your HIV and hepatitis B and C results must be negative to be in the study. If you are not selected to be in the study, for any reason, it is possible that we will not complete this testing on your blood. You can call the study staff to find out if your blood was tested for HIV and hepatitis B and C and the test results, if applicable.

5. GENERAL CLINIC RULES AND STUDY RESTRICTIONS

Meals and snacks will be served at scheduled times during your stay in the study clinic. You can eat only the food and drink provided to you. You can eat only at the times food is provided. You may be awakened during the night for scheduled events such as vital signs or blood draws.

Some drugs, foods, drinks, or activities can increase or decrease the effect of the study drugs. This can be a risk to your health or lead to false study results. Some of the restrictions and requirements for this study are listed below.

- You must be a non-smoker for the past 3 months.
- You must not have had an anaphylaxis, severe allergic reaction to tramadol, codeine, or other opioid drugs.
- If female you must not be pregnant or breast feeding.
- You must not have received another investigational agent within 4 weeks of Day -1, or received any other investigational agent during this study.
- You must not consume foods or beverages that contain alcohol within 24 hours of Day -1 until the end of the study.
- You must not consume foods or beverages that contains grapefruit, grapefruit-related citrus fruits (for example, Seville oranges, pomelos), or grapefruit juice or grapefruit-related juices within 7 days of the study drug dose and until the end of the study.
- You must not use prescription drugs (excluding birth control drugs or hormone replacement therapy) and nonprescription drugs, including dietary supplements and herbal remedies, from 14 days before Study Day -1 until the end of study (Study Day 11). Some drugs and substances may be restricted longer. The study staff can give you specific examples of these.
- You must not have elective surgical procedures at any time while on study.
- You must avoid severe physical exertion.

6. STUDY DRUG DOSING

The Study Doctor/study staff will let you know how much study drug you will receive prior to dosing.

You will take the following study treatments in random order. This means by chance, like flipping a coin. You will take each study treatment with a glass of water once during the study. Your mouth and hands will be checked to make sure you have swallowed the study treatment. You must not chew or crush the tablets. You must swallow them whole.

Study Treatment A: 30 mg desmetramadol (3 x 10 mg tablets) with food

Study Treatment B: 30 mg desmetramadol (3 x 10 mg tablets) without food

Study Treatment C: 10 mg desmetramadol (1 x 10 mg tablet) without food

Study Treatment D: 20 mg desmetramadol (2 x 10 mg tablets) without food

Study Treatment A Only:
You will fast (nothing to eat or drink, except water) for at least 10 hours until 30 minutes before dosing. At that time, you will be given a high-fat breakfast (containing pork and dairy products). You must eat the entire meal in 20 minutes or less. You will fast for another 4 hours after dosing.

7. POSSIBLE SIDE EFFECTS AND RISKS OF THE STUDY DRUG

If you do not understand what any of these side effects mean, please ask the Study Doctor or study staff to explain these terms to you.

Because this study drug is investigational, all of its side effects may not be known. There may be rare and unknown side effects. Some of these may be life threatening.

You must tell the study doctor or study staff about all side effects that you have. If you are not honest about your side effects, you may harm yourself by being in the study.

DESMETRAMADOL
Below is a list of the most common possible side effects of desmetramadol.

- Dizziness
- Sensation of Spinning or Whirling
- Incomplete or Infrequent Bowel Movements
- Headache
- Feel Like Throwing Up
- Throwing up
- Drowsiness
- Itching
- Nervousness and anxiety
- Weakness
- Lack of energy

- Sweating
- Indigestion (discomfort in the upper abdomen)
- Dry mouth
- Diarrhea (loose stools)

Below is a list of less common possible side effects of desmetramadol.

- General discomfort, illness, or unease
- Confusion
- Uncoordinated
- Intense excitement or happiness
- Very small eye pupils
- Poor sleeping
- Stomach pain
- Poor appetite
- Gas
- Tense, rigid muscles
- Rash
- Blurred vision
- Hot flashes, night sweats
- Incomplete urination

Below is a list of rare possible side effects of desmetramadol.

- Allergic reaction
- Suicide tendency
    - If you are having suicidal thoughts call the study doctor at the telephone number listed on the first page of this form. If you feel in crisis, you can call 911 and/or a Nationwide Suicide Hotline that is answered 24 hours a day with a skilled, trained counselor. One example is the National Suicide Prevention Lifeline at 1-800-273-TALK (8255).
- Weight loss
- Some or all of the following at the same time: altered thinking, increased reflexes, fever, shivering, shaking, agitation, sweating, seizures (as convulsions, sensory disturbances, or loss of consciousness), and coma (deep state of unconsciousness).
- Dizziness when sitting up or standing up
- Fainting
- Fast heart beat
- Difficulty breathing
- Hives (rash of round, red welts on the skin that itch)

Below is a list of very rare possible side effects of desmetramadol.

- Seizures (as convulsions, sensory disturbances, or loss of consciousness)
- Slow heart rate
- Low blood pressure

Because this study drug can cause drowsiness, dizziness, or blurred vision, if you experience any of these side effects you should use caution and for example avoid using stairs, driving a car, or working with machinery.

There is always a chance that an unexpected or serious side effect or allergic reaction may happen. This can happen to people who take this or any other drug. Some symptoms of allergic reactions are:

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

Please seek treatment immediately and tell the Study Doctor and study staff if you have any of these symptoms.

8. PROCEDURES AND POSSIBLE RISKS OR DISCOMFORTS

Procedures will be done during the study at assigned times. The procedures will be done to monitor your health, assess the safety of the study drug, and to see how the study drug is broken down in your body. You will be given a schedule of all study procedures.

A. BLOOD COLLECTIONS

A needle will be used to take blood samples from a vein in your arm about 62 times during the study. Less than 2 cups of blood will be taken. For additional information regarding blood volume please see study staff. Two cups is the amount you would give if you were donating blood. Additional samples may need to be taken.

You may have discomfort or pain when your blood is collected. You may feel faint or pass out. There is a risk of infection, bleeding, or bruising at the puncture site. You may develop a small scar at the puncture site where multiple blood samples are taken.

If the study staff has a difficult time obtaining your blood from the individual needle sticks you may be dropped from the study. On rare occasions, if blood cannot be obtained per the usual needle stick, we **may** place an IV (intravenous; in a vein) catheter (a small hollow tube) in a vein in your arm to obtain the blood. Blood is then withdrawn from a port on the IV at scheduled time points. The tube will be flushed or cleaned out with a small amount of saline (salt water) before and after it is used. You may have discomfort or pain when the IV is inserted. There is a risk of infection, bleeding and/or bruising at the insertion site.

B. URINE COLLECTION

Urine samples will be collected during the study. At certain times during the study all of your urine will be collected. During this time the restroom doors will be locked. You will contact the study staff each time you need to use the restroom. The study staff will provide you with a container and unlock the door for you. Urine collection is very important. You must follow the instructions of the study staff during this time.

C. VITAL SIGNS

Your vital signs will be measured at multiple times during the study. These include blood pressure, pulse rate, respiration rate, and body temperature (obtained by mouth).

D. PHYSICAL EXAM

A physical examination may be done.

E. FASTING RESTRICTION

You will be asked to fast at certain times during this study. This may cause discomfort.

F. PHOTOGRAPHS

If you develop a skin condition (reaction or rash) while being in this study, your skin condition may be photographed as soon as it is noticed and several other times until it is gone.

If the skin condition is on your face, all reasonable attempts will be made to disguise your facial features to hide your identity. It is possible that your face may be recognizable.

Your image may be sent electronically to the sponsor. The photographs or electronic images will be labeled with your study number and not your name. People working at Celerion, the Sponsor, the FDA, and IRB will have access to your photographs if they have a valid reason for seeing them. Valid reasons include but are not limited to, monitoring or auditing the study, to assess the skin condition or to determine the cause of the skin condition. When the study is over, your photograph or electronic image will be stored with the study files indefinitely. Your picture will not be used for teaching purposes and will not be published in any medical journal. You may be asked to have additional tests to assess the skin condition. The Study Doctor will discuss this with you before any other tests are done.

9. STUDY RE-CHECKS AND BLOOD EXPOSURE PROCEDURE

You may be asked to return to the clinic after the study is complete to follow up on abnormal laboratory tests. The study staff may also call you to follow up on any unresolved adverse events. It is important for your safety that you comply with study staff requests to return and/or respond to any telephone calls. You may not be able to do future studies if we are unable to ensure that all your abnormal results have returned to acceptable levels and all of your adverse events have resolved.

If a study staff member sustains an exposure to your blood, tissue or body fluids by needle stick, cut or splash to mucosa or damaged skin, your name, address, telephone and date of birth will be given to the private doctor who is treating the study staff member. You may be contacted in order to collect your blood or to ask your permission to use an existing blood sample to test for HIV and hepatitis B and C. If your blood is tested, you will receive a copy of the results.

This is to enable the study staff member to receive appropriate counseling, monitoring and treatment if necessary. If your blood tests positive the results will need to be reported to the local health authorities.

10. UNKNOWN RISKS

There is always a chance that an unexpected or serious side effect may happen. This can happen to people who take this or any other drug. You must report any new symptoms/signs of illness to the study nurses any time after you have signed and dated this Informed Consent Form.

11. POSSIBLE RISKS TO AN UNBORN BABY OR CHILD WHO IS BREASTFEEDING

The risks of using desmetramadol during pregnancy are not known. It is possible that this study drug may cause harm to an unborn baby. This includes death, congenital malformations or other unforeseen health problems for the baby.

If you are able to become pregnant you must use one or more of the following forms of birth control from screening, throughout the study, and for 30 days following the study drug dose.

- Hormonal (for example, oral, transdermal, intravaginal, implant or injection for 3 months)
- Double barrier (for example, condom or diaphragm with spermicide)
- Intrauterine device (IUD) or system (IUS) (for 3 months)
- Vasectomized partner (6 months minimum)
- Abstinence (not having sex)

If you become pregnant during the study, you must tell the Study Doctor or study staff right away. The Study Doctor will ask if the pregnancy can be followed to the outcome.

If the partner of a male participant were to become pregnant during the study, you must tell the Study Doctor or study staff right away. Your partner will be asked to allow the study team to follow her pregnancy to outcome.

12. SIGNIFICANT NEW SAFETY FINDINGS DURING THE STUDY

You will be told of any significant new safety findings that Celerion is made aware of by the Sponsor that might influence your willingness to continue your participation in this study.

13. POSSIBLE BENEFITS FROM THE STUDY

You will not receive any health benefits from being in this study. The tests provided may help you learn about your general health. They may also help you discover an unknown medical condition. This study may help doctors and scientists learn things about the study drug that will help others.

14. TAKING PART IN THE STUDY OF YOUR OWN FREE WILL

You are being asked to take part in this study because you are healthy. You will not be taking the study drug to treat any disease or condition. The only other option is not to take part in this study.

You will take part in the study by your own choice and your own free will. No one can force you to be in the study. If you enter the study, no one can force you to stay in the study. If you choose not to be in the study or if you leave the study early, there will be no penalty or loss of benefits. **If you leave or are removed from the study for any reason your stipend will be prorated to the amount of the study that you complete.** You will not lose any rights that you are entitled to as a research subject.

15. COST AND PAYMENT FOR TAKING PART IN THE STUDY

There are no costs to you for being in the study. The study drug and study procedures are provided to you at no charge.

Celerion will pay you via the payment method you select, based upon the information provided by study staff, within 7 days following completion of the study. The amount you will be paid will depend on how much of the study you complete. You will earn $2,880 if you complete the confinement period (your stay in the clinic). You will earn a completion bonus ($720) if you complete the entire study. You will be paid a total of $3,600 for completing the entire study.

If you leave the study early, you will receive a pro-rated amount based on the study days you completed. If you complete an unscheduled study return visit you will be paid $150 for travel and time.

To ensure that the study doses the required number of subjects, extra subjects are recruited. These extra subjects are called alternates. If you are randomly chosen to be an alternate you will be told after you check in to the clinic. As an alternate you will be asked to complete study procedures up to the time of dosing. In the event that an on study subject is unable to dose, you may be chosen to take that subject's place on the study. If you are not needed, you will be released from the clinic after dosing. If you complete all the alternate requirements, you will receive an alternate stipend of $360 within approximately 1 week after being released from the clinic. If you are an alternate or a study subject who is released prior to the initial dosing you will receive a prorated portion of the alternate stipend (or $150 minimum) based on the amount of the study that you complete.

Celerion will pay you an additional $250 if the study schedule requires that you return, check-in or are confined to the site on any of the following holidays: Easter Sunday, Memorial Day, July 4th, Labor Day, Thanksgiving, Christmas Eve Day, Christmas Day, New Year's Eve Day, New Year's Day. You must complete the holiday return/confinement (on the actual holiday) in order to receive this additional holiday stipend.

You understand the following:

- No deductions will be withheld from your stipend payment for tax purposes. You are responsible for reporting any payment on your state and federal tax returns. At the end of each year, Celerion will notify the IRS of all stipends you have received throughout the year.
- You will be paid through a payment vendor selected by Celerion in the method you select from the available payment options.

- In order to be paid through the payment vendor, information such as your name, home address, email address, phone number, and date of birth will be provided to Celerion's vendor. Once you have access to the vendor's pay portal, you will need to provide your social security or tax identification number and the vendor may request that you provide additional information based upon the payment method you select. All of your personal information that Celerion provides to the vendor will be handled in accordance with the confidentiality and privacy section. The vendor's privacy policy is also available to you on the website and through the payment portal.
- Being in this study does not make you an employee of the Sponsor, Celerion, or the FDA.
- You will not receive the full payment for the study if you leave before it is complete or are removed from the study for any reason. **This includes leaving the study due to an adverse event.**

16. COMPENSATION FOR AN INJURY DIRECTLY RELATED TO YOUR PARTICIPATION IN THIS STUDY

There is a chance that you could become ill or injured while being in this study. Celerion will help you make arrangements if your illness or injury requires care outside of Celerion (hospital, medical specialist). Unless other arrangements have been made by Celerion, all billing will be under your name. The cost of this care will be billed to you or your insurer in the ordinary manner. If you do not have insurance, the cost of the care will be billed to you directly.

The Study Doctor will decide if an injury or illness is directly related to the performance of the protocol (study plan) or use of the study drug. If your injury or illness is directly related to the performance of the protocol or use of the study drug, the Sponsor and/or Celerion will reimburse you for your reasonable out-of-pocket medical costs (not covered by insurance) to treat a study-related illness or injury.

To pay these medical expenses, the Sponsor will need to know some information about you like your name, date of birth, and social security number or Medicare Beneficiary Identifier (MBI). This is because the Sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

You will need to sign a "release of information" form. This form will allow Celerion to obtain your medical records related to the illness or injury. These records will help the Study Doctor determine the cause of the illness or injury. They may also help the Sponsor learn more about the safety of the study drug.

Any injury or illness that is not directly related to the performance of the protocol or use of the study drug will be your responsibility to pay and to follow up with your private doctor or clinic. This includes any injury or illness that would have occurred even if you had not participated in the clinical trial.

In no way does signing and dating this consent form waive your legal rights nor does it relieve the Study Doctor, Sponsor or involved institutions from their legal and professional responsibilities.

17. REASONS YOU CAN BE REMOVED FROM THE STUDY

You can be removed from the study at any time and for any reason without your consent. Some of the reasons you can be removed are listed below.

- You do not follow the instructions, rules, and restrictions given by the study staff.
- You do not continue to meet the requirements for the study.
- The Study Doctor decides it is best for your health.
- The Sponsor stops the study or asks that you be removed from the study.
- You become pregnant.
- You vomit at certain times during the study.
- You have excessive diarrhea (loose stool).

18. LEAVING THE STUDY BEFORE IT IS COMPLETED

Leaving the study before it is complete may be harmful to your health. If you choose to leave the study, you must notify the study staff. It is very important that you agree to have the following procedures completed. The procedures will be done for your safety and well-being.

- Vital Signs
- Provide blood samples
- Record any side effects you may have or medications you have taken.

All data that has been collected from you will be used for its original intention. If you leave the study early or you are removed from the study, all samples collected from you before you leave will be used and analyzed as described in this consent.

19. CONFIDENTIALITY, DATA PROTECTION, AND PRIVACY

Information collected about you and your participation in this study, including all medical and health information as outlined below, will be kept confidential according to privacy laws in this country. The information in both paper and electronic format that Celerion will collect about you will include study records that may contain your name and other personally identifiable information (PII) such as your date of birth. PII is information that directly identifies you, and will also include special information such as your racial or ethnic origin, physical or mental health, sexual life, or genetic data and/or biometric data for the purpose of uniquely identifying you. These records (including any photographs) containing your PII will be kept for a minimum of either two years following the approval of the study drug, or two years after the Sponsor discontinues its research on the study drug, and may be kept for as long as the Sponsor is developing or commercializing the study drug, which may be indefinitely. Your study results will be coded with numbers and/or initials wherever possible. Celerion will keep a list that links your name to your study results. This list will be kept confidential, however it may be provided to the Sponsor and third parties listed below. Celerion may share your PII among Celerion affiliates who are located in other countries around the world. All Celerion affiliates will comply with the terms of this ICF and all Celerion policies and applicable laws and regulations at all times with respect to your PII.

The study results, including your PII, may be disclosed to, audited by, and/or monitored by the people listed below. This is to analyze the study data for the purposes of

development and/or commercialization of the study drug, and also to make sure the study was done correctly. In order for this to take place, some third parties will have direct access to your PII, and may copy some of the original records that contain your PII. This includes the laboratory report linking your name to your HIV and/or hepatitis test results. Your original records maintained by Celerion and accessed by the people listed below may contain your PII. PII may be disclosed to the third parties listed below as necessary with respect to any investigation, complaint, or claim, including with respect to any investigation by a governmental authority. These third parties include:

- Regulatory authorities, such as the FDA, MHRA (Medicines and Healthcare products Regulatory Agency), EMA (European Medicines Agency) or Health Canada
- The Sponsor and third parties working with the sponsor
- Celerion and third parties working with Celerion
- The Institutional Review Board (IRB is a group of people who review research studies to protect the rights and welfare of research subjects.)

All of the parties listed above will maintain, use, disclose, transfer and access your PII confidentially and in accordance with applicable law or regulation.

Under certain circumstances, some test results will be reported to health and regulatory authorities. This is done when required by law or regulation. If a medical emergency happens, your study results, including your PII, may be given to emergency medical staff not employed by Celerion or the Sponsor.

In addition to the purposes outlined above, Celerion or the Sponsor may utilize your study results, including your PII, for publication purposes, such as presenting on the study results at a conference, publishing in a medical book or journal, writing a white paper about the study, or used for teaching purposes. In the event of any such publication, your PII will be anonymized prior to disclosure to third parties. Neither your name nor other identifiers will be used in any publication or teaching material. Further, Celerion may use your PII to make automated decisions, such as whether or not you are eligible to participate in any other study at Celerion.

You may withdraw your consent from Celerion’s collection, use, processing, disclosure, and onward transfer of your PII at any time. If you withdraw your consent, Celerion will not collect any further PII about you except as may be necessary to follow-up on any safety events that may have occurred while you were taking part in the study or as otherwise described in this Informed Consent Form, and you may be removed from the study. Any PII, information, and samples collected from you during any follow-up visits after you withdraw your consent will also remain part of the study. The data collected from you during your participation in the study cannot be deleted even if you stop participating in the study. In addition, any PII, information, and samples collected in connection with the study will remain part of the study after your participation has ended in order to guarantee the validity of the study and to comply with legal and regulatory requirements for obtaining drug authorization and approval. If you request that your PII be erased, the PII already gathered will also still be kept in the study database as necessary to comply with all laws and regulations applicable to clinical trials, however all

other PII will be erased from our databases where allowed by applicable law and regulation. Any PII that cannot be erased will be used as described in this Informed Consent Form. In accordance with applicable law, you may request (in writing) to see or have a copy of the study data collected about you. You have the right to request a correction to any PII about you that is not correct. You may not be able to see some data until after the study is over.

By signing and dating this form, you are allowing the collection, processing, use, disclosure, and onward transfer of your PII as described in this consent.

If you have any questions or concerns about Celerion's collection of your PII or the information outlined in this ICF, you may contact the Celerion Privacy Officer by electronic message at privacy@celerion.com; or by mail at 621 Rose Street, Lincoln, NE 68502. In addition, you have the right to lodge a complaint with any applicable governmental authority if you believe we have not complied with the requirements of applicable law with regard to your PII.

20. WHOM TO CONTACT ABOUT THE STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject and/or concerns or complaints regarding this research study, contact:

- By mail: Study Subject Adviser
  Advarra
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00033544.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov. 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.

See Next Page

21. YOUR CONSENT

Your signature below verifies that:

- You have had adequate time to read this written Informed Consent Form.
- A study staff member has explained this form to you.
- You have had the chance to ask questions about the study.
- All of your questions have been answered.
- You understand the information in this Informed Consent Form.
- You agree to follow the restrictions of the study.
- You agree to take part in the study and give your consent for study procedures.
- You are aware that nothing contained in this Informed Consent Form waives any of your legal rights as a research subject, nor does it release the Study Doctor, the Sponsor, Celerion, or its agents from any liability for negligence.

Would you like Celerion to inform your healthcare provider of your participation in this study? Check one: Yes ☐ No ☐

Name of healthcare provider:_____

Address of healthcare provider:_____

Subject Name (Print):_____

Subject Signature:_____ Date:_____

22. FOR CELERION STUDY STAFF

I have discussed this study with the above subject. This person had an opportunity to ask questions. The Subject signed and dated in my presence.

Signature:_____ _____ _____
(Study Staff Member explaining study and ICF) Date Time

23. ACKNOWLEDGEMENT

You have been given a signed and dated copy of this document. Initials_____