INFORMED CONSENT FORM

Sponsor: **Virogenics, Inc.**

Study Title: **A First-in-Human, 4-Part, Randomized, Double-Blind, Placebo-Controlled, Single Ascending Dose, Multiple Ascending Dose, and Food-Effect Study to Assess the Safety, Tolerability, and Pharmacokinetics of CMS121 Administered Orally to Healthy Young and Elderly Adult Subjects**

Study Doctor: **Scott Rasmussen, 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 Virogenics, Inc. Celerion is being paid by Virogenics 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, CMS121, is experimental. That means the United States Food and Drug Administration (FDA) has not approved it for sale or use. CMS121 is being studied to treat Alzheimer's disease (AD).

This is the first study in which CMS121 will be given to humans.

The purposes of this study are to:

Part 1 Single Ascending Dose (SAD)

- Learn about the safety of a single oral dose of CMS121 (at doses that ascend—or increase—in size) in healthy young adult subjects.

- Learn how subjects tolerate a single oral dose of CMS121 (at doses that ascend—or increase—in size) in healthy young adult subjects.
- Find out how much CMS121 (and/or CMS121 breakdown products) is in the blood and urine of healthy subjects after a single oral dose of the study drug.
- Learn how CMS121 affects the heart after a single oral dose of the study drug.

Part 2 Multiple ascending dose (MAD)

- Learn about the safety of multiple (7) oral doses of CMS121 (at doses that ascend—or increase—in size) in healthy young adult subjects.
- Learn how subjects tolerate multiple (7) oral doses of CMS121 (at doses that ascend—or increase—in size) in healthy young adult subjects.
- Find out how much CMS121 (and/or CMS121 breakdown products) is in the blood and urine of healthy subjects after taking single (1) and multiple (7) oral doses of CMS121.
- Learn how CMS121 affects the heart after multiple (7) oral doses of the study drug.

Part 3 (Elderly)

- Learn about the safety of multiple (7) oral doses of CMS121 in healthy elderly subjects.
- Learn how subjects tolerate multiple (7) oral doses of CMS121 in healthy elderly subjects.
- Find out how much CMS121 (and/or CMS121 breakdown products) is in the blood and urine of healthy elderly subjects after taking multiple oral doses of CMS121.

Part 4 Food Effect (FE)

- Learn about the safety of a single oral dose of CMS121, given with and without food, in healthy young adult subjects.
- Learn how subjects tolerate a single oral dose of CMS121, given with and without food, in healthy young adult subjects.
- Find out how much CMS121 is in the blood of healthy young adult subjects after taking a single oral dose of CMS121 with and without food.

2. NUMBER OF SUBJECTS AND LENGTH OF STUDY

This study will enroll about 100 subjects. There are 4 parts to this study and you will only be in 1 part.

Part 1 (SAD)
The entire study will last about 9 days plus up to 28 days for screening. There is 1 confinement period when you will stay in the clinic the entire time. The confinement period will last about 5 days. There is 1 return visit to the clinic.

Parts 2 & 3 (MAD and Elderly)
The entire study will last about 15 days plus up to 28 days for screening. There is 1 confinement period when you will stay in the clinic the entire time. The confinement period will last about 11 days. There is 1 return visit to the clinic.

Part 4 (FE)
The entire study will last about 19 days plus up to 28 days for screening. There are 2 confinement periods when you will stay in the clinic the entire time. The confinement periods will last about 5 days. There is 1 return visit to the clinic.

3. 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 (for example, 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 and cotinine (nicotine exposure). If you are female, your blood will be used for a pregnancy test or a follicle stimulating hormone (FSH) test to determine if you are post-menopausal
- 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.

4. 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.

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 may increase or decrease the effect of the study drug. This might be a risk to your health or lead to false study results. Some of the restrictions and requirements for this study are listed below.

All Parts:

- You must be a continuous non-smoker who has not used nicotine-containing products for at least 3 months prior to the first dosing and throughout the study.
- You must not be pregnant or breastfeeding.
- You must be able to swallow multiple capsules.
- You must not have any condition (for example, chronic diarrhea) or prior surgery (for example, gastric bypass) that could interfere with drug absorption, distribution, metabolism, or excretion.
- You must not have a clinically significant surgical procedure within 90 days prior to the screening visit.
- You must not have a clinically significant acute illness or infection within 14 days prior to the first dosing.
- You must not consume excessive amounts alcohol, defined as weekly intake in excess of 14 units of alcohol (1 unit = 12 fluid ounces of beer, 5 fluid ounces of wine, or 1.5 fluid ounces [1 shot] of distilled spirits or liquor), within 6 months prior to the screening visit.
- You must not consume excessive amounts of caffeine (defined as consuming greater than 5 servings of caffeinated beverages [for example, coffee, tea, cola, energy drinks] per day).
- You must not consume foods or beverages containing grapefruit/Seville orange within 14 days prior to first dosing and until the last blood sample collection.
- You must be able to avoid exposure to natural or artificial sunlight (tanning beds or ultraviolet [UV] A/B treatment) for 72 hours following last dosing. You should use a sunscreen and/or wear a hat and clothes that cover your skin if you have to be in sunlight during this time period.
- You must not have been on a diet that conflicts with the on-study diet within the 30 days prior to the first dosing.
- You must not have used any investigational drug or device within 30 days or biologics for 90 days prior to the first dosing, or currently participating in another study of an investigational drug or biologics, or a medical device.
- You must not have donated or had a blood loss of greater than 500 mL (about 2 cups) within 56 days prior to study drug dosing.

- You must not have donated plasma within 30 days prior to the first dosing.
- You must not be an employee or family member of the Study Doctor, study staff, or Sponsor.
- You must refrain from strenuous physical activity which could cause muscle aches or injury, including contact sports at any time from the screening visit until completion of the study.

Parts 1 (SAD) and 2 (MAD)

- You must not use any drugs, including prescription and non-prescription drugs, herbal remedies, or vitamin supplements beginning 14 days prior to the first dosing. Some drugs and substances may be restricted longer than 14 days. The study staff can give you specific examples of these.
- You must not have an allergy to band aids, adhesive dressing, or medical tape.
- You must not consume foods or beverages containing other fruit juice within 72 hours prior to first dosing and until the last blood sample collection.
- You must not consume foods or beverages containing xanthines/caffeine within 24 hours prior to first dosing and until the last blood sample collection.
- You must not consume foods or beverages containing alcohol within 48 hours prior to first dosing and until the last blood sample collection.

Part 3 (Elderly)

- You must not use any drugs, including prescription and non-prescription drugs, herbal remedies, or vitamin supplements beginning 14 days prior to the first dosing. Thyroid hormone replacement drugs will be allowed if you have been on the same stable dose for at least 3 months prior to first dosing. Certain hormonal therapies/birth control methods may also be allowed. Some drugs and substances may be restricted longer than 14 days. The study staff can give you specific examples of these.
- You must not consume foods or beverages containing other fruit juice within 72 hours prior to first dosing and until the last blood sample collection.
- You must not consume foods or beverages containing xanthines/caffeine within 24 hours prior to first dosing and until the last blood sample collection.
- You must not consume foods or beverages containing alcohol within 48 hours prior to first dosing and until the last blood sample collection.

Part 4 (FE)

- You must not be lactose intolerant (the inability to digest a sugar called lactose that is found in milk and dairy products).

- You must not use any drugs, including prescription and non-prescription drugs, herbal remedies, or vitamin supplements beginning 14 days prior to the first dosing. Certain hormonal therapies/birth control methods may be allowed. Some drugs and substances may be restricted longer than 14 days. The study staff can give you specific examples of these.

- You must be able to completely consume a standardized high-fat/high-calorie breakfast.

- You must not consume foods or beverages containing other fruit juice within 72 hours prior to each dosing and until the last blood sample collection in each study treatment period.

- You must not consume foods or beverages containing xanthines/caffeine within 24 hours prior to each dosing and until the last blood sample collection in each study treatment period.

- You must not consume foods or beverages containing alcohol within 48 hours prior to each dosing and until the last blood sample collection in each study treatment period.

6. STUDY DRUG DOSING

Parts 1, 2, and 3
You will be enrolled into a study dose level group. In each study dose level group, you will be randomly assigned (by chance, like flipping a coin) to take CMS121 or placebo. Out of 8 subjects in each dose level group, 6 will receive CMS121 and 2 will receive placebo. A placebo is a capsule that looks just like the CMS121 capsule but contains no study drug. The use of a placebo helps to make sure that any side effects during the study are judged fairly. Neither you nor the study staff will know who is taking CMS121 and who is taking placebo. If necessary for safety reasons, the Study Doctor can find out which study dose level you were assigned to. When you take the study drug, your mouth and hands will be checked to make sure you have swallowed the capsule. You must not crush, split or chew the capsule.

The Study Doctor and the Sponsor will review the safety data of each dose level. The next dose level will not be dosed until the safety data has been reviewed. The doses maybe modified at any time during the study based on the safety and tolerability of the study drug. The Sponsor and/or the Study Doctor can stop the study at any time.

The Study Doctor/study staff will not tell you if you are receiving CMS121 or placebo, but they can let you know what dose of CMS121 is being used in your study dose level group prior to dosing.

Part 1 (SAD)
CMS121 or matching placebo capsule will be taken only once on Day 1.

- Study Dose Level S1: 50 mg CMS121 or matching placebo capsule
- Study Dose Level S2: 150 mg CMS121 or matching placebo capsule

- Study Dose Level S3: 300 mg CMS121 or matching placebo capsule
- Study Dose Level S4: 600 mg CMS121 or matching placebo capsule
- Study Dose Level S5: 1200 mg CMS121 or matching placebo capsule
- Study Dose Level S6: 1800 mg CMS121 or matching placebo capsule

Part 2 (MAD)
CMS121 or matching placebo capsule will be taken every day for 7 days (Days 1 to 7).

- Study Dose Level M1: 150 mg CMS121 or matching placebo capsule
- Study Dose Level M2: 300 mg CMS121 or matching placebo capsule
- Study Dose Level M3: 600 mg CMS121 or matching placebo capsule
- Study Dose Level M4: 900 mg CMS121 or matching placebo capsule

Dose level in each cohort may be adjusted based on emerging data available from Part 1 and available data from previous groups in Part 2.

Part 3 (Elderly)

CMS121 or matching placebo capsule will be taken every day for 7 days (Days 1 to 7).

The dose level will be determined based on emerging data available from Parts 1 and 2.

Part 4 (Food Effect)
The dose level will be determined based on emerging data available from Part 1. The Study Doctor/study staff will let you know how much study drug you will receive before dosing.

You will receive a single oral dose of CMS121 on Day 1 of each period. There will be two dosing periods. You will receive a total of two doses of CMS121, one dose with food and one dose without food.

You will take CMS121 with food or without food in random order. Random means by chance, like flipping a coin. You will take each capsule with a glass of water. Your mouth and hands will be checked to make sure you have swallowed the capsule. You must not crush, split or chew the capsule.

Study Treatment A (Fed): To Be Determined (TBD) mg CMS121 with food

Study Treatment B (Fasting): (TBD) mg CMS121 without food

All Parts:
Additional groups may be enrolled if it is deemed appropriate to repeat any dose level, or to add dose level(s), as determined by the Sponsor in consultation with the Study Doctor, depending on the safety and tolerability results from the prior groups(s).

Part 1:
You will fast (nothing to eat or drink, except water) for at least 10 hours until about 30 minutes before dosing. At that time, you will be given a light breakfast (may contain pork and dairy products). You must try to eat the entire meal in 30 minutes or less. You will fast for at least 4 hours after dosing.

Parts 2 and 3:
On Days 1 and 7 you will fast (nothing to eat or drink, except water) for at least 10 hours until about 30 minutes before dosing. At that time, you will be given a light breakfast (may contain pork and dairy products). You must try to eat the entire meal in 30 minutes or less. You will fast for at least 4 hours after dosing. For all other morning doses (Days 2-6), you will be required to fast for at least 1 hour until about 30 minutes prior to your scheduled morning dose, when you will be given a light breakfast and will fast for at least 2 hours after dosing.

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

For Study Treatment B, you will fast overnight for at least 10 hours prior to dosing and will continue the fast for at least 4 hours after dosing.

POSSIBLE SIDE EFFECTS RELATED TO THE STUDY DRUG:
This is the first study of CMS121 (the study drug) in humans. So, we don't know what side effects the study drug may cause in humans. In an attempt to avoid side effects, this study will only use doses of study drug that did not cause side effects in animals. At doses higher than those planned for this study, animals experienced loss of appetite, weight loss, vomiting, loose stools, and changes in kidney appearance (under the microscope) and blood tests of kidney health.

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 may include but are not limited to:

- 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 or study staff if you have any of these symptoms.

7. 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

Part 1
A needle will be used to take blood samples from a vein in your arm about 19 times during the study. Less than 2 cups of blood will be taken.

Parts 2 and 3
A needle will be used to take blood samples from a vein in your arm about 34 times during the study. Less than 2 cups of blood will be taken.

Part 4
A needle will be used to take blood samples from a vein in your arm about 36 times during the study. Less than 2 cups of blood will be taken.

All Parts
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 intravenous (IV) catheter in a vein. A 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. FUTURE RESEARCH

Any residual plasma and urine from the blood samples will be stored by the Sponsor or bioanalytical facility for up to 5 years after the last dosing and may be used for future analyses (for example, blood assessment, metabolic profiling). Tubes will be identified with a barcode using an appropriate label. No diseases/conditions, deoxyribonucleic acid (DNA), or ribonucleic acid (RNA) will be the focus of these analyses. The analyses will only focus on analytes/biomarkers. Samples will not be submitted to a public database. The Sponsor and contract research organizations involved in the clinical conduct, bioanalytical analyses and blood and statistical analyses of the data will have access to the samples and /or the data that resulted from the analyses, if performed. By signing and dating the informed consent form (ICF), you agree to the possible future analysis of these samples. At any time, you can contact the study staff to requested destruction of the residual samples after the blood assessments required to meet the primary objective of the study are completed. Any additional research on these samples unspecified by this protocol will require approval from you.

C. URINE COLLECTION (PARTS 1 AND OPTIONAL IN PARTS 2 AND 3)

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.

D. VITAL SIGNS

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

E. ECG

ECGs (electrocardiograms) will be done. An ECG traces the electrical activity of the heart. You may have mild irritation, slight redness, or itching at the sites on your skin where the adhesive (sticky) recording patches are placed. If male, it may be necessary to shave the area on your chest for placement of ECG tabs directly on skin.

F. HOLTER MONITOR (PARTS 1 AND 2 ONLY)

A holter monitor is a small battery-powered recorder that will monitor and record the electrical activity of your heart continuously while you go about your usual daily activities. The recording device of a holter monitor is worn on a strap at your waist or over your shoulder. The electrical signals of your heart are picked up by two small metal pads (electrodes) attached to your chest (held in position with sticky tape) which are connected to the recorder by wires. Holter monitoring has no known risks but can feel uncomfortable and may restrict some of your daily activities.

G. WEIGHT

Your weight will be taken.

H. PHYSICAL EXAM

Physical examinations will be done.

I. FASTING AND CAFFEINE RESTRICTION

You will be asked to fast at certain times during this study. You will not be able to ingest caffeine containing foods and beverages. This may cause discomfort.

J. COLUMBIA SUICIDE SEVERITY RATING SCALE (C-SSRS) (PARTS 2 AND 3 ONLY)

This questionnaire will assess your mood and behavior. In addition, if at any time during the study, you experience suicidal thoughts or suicidal behavior, you must tell the Study Doctor and/or study staff right away. You will be asked questions about personal issues during this study. There may be questions about your mood, sexual functioning, drug use, etc. These types of personal questions may make you uncomfortable. If you feel in crisis, you can talk to the Study Doctor/study staff, call 911 and/or call a Nationwide

Suicide Hotline that is answered 24 hours a day with a skilled, trained counselor. One example hotline is the National Suicide Prevention Lifeline at 1-800-273-TALK (8255).

K. PHOTOGRAPH

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.

8. 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.

9. 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.

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

The risks of using CMS121 during pregnancy are not known. It is possible that this study drug may cause harm to an unborn baby. This includes death, birth defects, or other unforeseen health problems for the baby.

Females
If you are able to become pregnant and ever engage in heterosexual (someone of the opposite sex) relationships, you must agree to use one highly effective form of birth control or two effective forms of birth control for 28 days prior to the first dosing and throughout the study.

Highly effective forms of birth control include:

- Copper intrauterine device (IUD)—acceptable in Study Parts 1 to 4
- Progesterone IUD—acceptable in Study Parts 3 and 4
- Etonorgestrel implant—acceptable in Study Parts 3 and 4

Effective forms of birth control include:

- Vaginal (that is, female/internal) condoms* with spermicide (considered dual birth control)—acceptable in Study Parts 1 to 4
- Penile (that is, male/external) condoms* with spermicide (used by partner, considered dual birth control)—acceptable in Study Parts 1 to 4
- Vaginal sponge with spermicide—acceptable in Study Parts 1 to 4
- Diaphragm with spermicide—acceptable in Study Parts 1 to 4
- Intravaginal hormonal/birth control ring—acceptable in Study Parts 3 and 4
- Transdermal hormonal/birth control patch—acceptable in Study Parts 3 and 4
- Oral hormonal/birth control drugs—acceptable in Study Parts 3 and 4

*Note: It is never acceptable to use a vaginal and penile condom together, as the friction between the two condoms can cause tearing and failure of one or both condoms.

You must not donate oocytes (eggs) from the first dosing until 28 days after your last dose of study drug.

If you are able to become pregnant and engage in heterosexual relationships you must continue the same birth control method(s) for at least 28 days after the last dosing.

Males
If you ever engage in heterosexual (someone of the opposite sex) relationships and you have not had a vasectomy (*at least 4 months* prior to first dosing), you must agree to use one of the following methods of birth control during the study until 90 days after the last dosing:

- Penile (that is, male/external) condoms* with spermicide
- Vaginal (that is, female/internal) condoms* with spermicide
- Abstain from sexual intercourse

*Note: It is never acceptable to use a vaginal and penile condom together, as the friction between the two condoms can cause tearing and failure of one or both condoms.

You must agree not to donate sperm from the first dosing until 90 days after the last dosing.

11. 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.

12. 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.

13. 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.

14. 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. The amount you will be paid will depend on how much of the study you complete.

Part 1:
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.You will earn $150 if you complete the study confinement check-in day. You will earn $435 for each of the three full study confinement days that you complete. You will earn $150 if you complete the study confinement check-out day. You will earn $150 for the final study return visit that you complete. You will earn a completion bonus ($445) if you complete the entire study. You will be paid a total of $2,200 for completing the entire study.

Part 2:
You will earn $150 if you complete the study confinement check-in day. You will earn $410 for each of the nine full study confinement days that you complete. You will earn $150 if you complete the study confinement check-out day. You will earn $150 for the final study return visit that you complete. You will earn a completion bonus ($1,060) if you complete the entire study. You will be paid a total of $5,200 for completing the entire study.

You will receive a partial payment at the times listed below:

- $3,990 within 7 days following completion of the study confinement
- $1,210 within 7 days following completion of the final study return visit

Part 3:
You will earn $150 if you complete the study confinement check-in day. You will earn $410 for each of the nine full study confinement days that you complete. You will earn $150 if you complete the study confinement check-out day. You will earn $150 for the final study return visit that you complete. You will earn a completion bonus ($1,060) if you complete the entire study. You will be paid a total of $5,200 for completing the entire study.

You will receive a partial payment at the times listed below:

- $3,990 within 7 days following completion of the study confinement
- $1,210 within 7 days following completion of the final study return visit

In addition to the above, if you complete any screening procedure you will earn a screening stipend of $150.

Part 4:
You will earn $150 for each of the two study confinement check-in days you complete. You will earn $435 for each of the six full study confinement days that you complete. You will earn $150 for each of the two study confinement check-out days you complete. You will earn $150 for the final study return visit that you complete. You will earn a completion bonus ($840) if you complete the entire study. You will be paid a total of $4,200 for completing the entire study.

You will receive a partial payment at the times listed below:

- $1,605 within 7 days following completion of the first study confinement

- $1,605 within 7 days following completion of the first study confinement
- $990 within 7 days following completion of the final study return visit

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 $220 (Part 1), $520 (Part 2 and Part 3), and $420 (Part 4) within 7 days 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.**

15. 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.

16. 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.
- Difficulties with blood collection.
- You become pregnant.

17. LEAVING THE STUDY BEFORE IT IS COMPLETED

You are free to leave the study at any time. 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.

- Physical examination
- ECG
- Weight
- Vital Signs
- Provide blood and urine samples
- Record any side effects you may have or medications you have taken.
- Follow-up return visit about 7 days after you leave the study

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.

This study drug may affect your coordination and your ability to think. It may not be safe for you to perform certain tasks. For 24 hours after taking the study drug you should avoid the following:

- Driving a car
- Operating machinery
- Using power tools or equipment
- Activities or things that require mental alertness

18. 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.)
- Representatives of the National Institutes of Health, which is the financial sponsor of the study

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.

19. VERIFIED CLINICAL TRIALS (VCT)

In order to determine if you may be eligible to be in a research study, it is necessary to know if you are currently or have recently been in a research study. Celerion uses the VCT database to help determine this. You are being asked to agree to permit Celerion to check the VCT database that contains clinical trial information about subjects who are in research studies. You may be in this VCT database if you have already given permission to another research site. VCT is a secure internet-based registry of research subjects. The registry stores specific information regarding a research subject's participation at various clinical trial sites. VCT is a privately-owned company and has an agreement with Celerion to run this registry. VCT does not take part in the performance of the study or in the operation of Celerion.

Information such as your name will be entered into the VCT system with or without your fingerprint. The VCT system de-identifies your partial name identifiers and creates a unique identification code (UIC). This means that by looking at the code you would not be able to tell what the person's name is or their private information. The UIC is created by information entered into the database: name, date of birth, gender, and digits of valid ID numbers such as driver's license number, passport number, cedula number or military ID number, and state or country of issue. If fingerprint is used, the actual fingerprint is not collected nor stored. Only a portion of the fingerprint is used and again is de-identified.

If you enroll in this research study, Celerion will include in the database information that you are enrolled in a research study.

Your confidentiality will be respected and no information that discloses your identity will be released or published without your authorization, except as described in this form and unless required by law. The data contained in this registry will be stored securely by VCT, and accessed by Celerion staff and authorized VCT personnel.

Your information may be used and shared with these people for the following purposes:

- The Study Doctor and study staff to help determine whether you are eligible for this particular research study

- Study Doctors and study staff members at other study centers who may access the database to help determine whether you are eligible for future research studies
- VCT for maintaining its database and working with clients

After your information is shared with the people and companies listed above, the law may not require them to protect the privacy of your information.

You have the option to review your personal information in the database. You may inquire about your personal information in the database at any point in time by contacting Verified Clinical Trials at 516-998-7499.

There is no anticipated potential risk for physical or medical harm by taking part in the VCT registry. There is a risk that your information may be released accidentally. There is no way to guarantee absolute confidentiality.

You may withdraw your personal identifiable information (partial name, date of birth, partial ID information) from the VCT registry at any time without penalty or loss of benefits. However, your ability to enroll or continue in the clinical trial that you are screening for may require your participation in this registry. Although you withdraw your personal information from the registry and delete your personal information, your de-identified UIC and de-identified fingerprint code (connected to your study history) will remain in the VCT system.

Your information will remain in the VCT database for a period of up to 50 years, at which point it will be destroyed. To remove your personal identifiable information from the VCT database, please contact VCT at 516-998-7499 or in writing that you no longer wish to have your personal information stored with VCT. VCT's mailing address is Verified Clinical Trials, 1305 Franklin Avenue, #150, Garden City, NY 11530. VCT's email address is info@verifiedclinicaltrials.com. This authorization expires in 50 years.

If you are concerned that the information in the database about your participation in clinical research studies is not accurate, you can contact VCT at any time at 516-998-7499.

By signing and dating this Informed Consent Form, you authorize the collection, use and/or disclosure of your partial personal information as described above. This information may be disclosed by either Celerion or by VCT if such disclosure is permitted or required by law.

The personal information which you provide will be stored in the VCT database. The database is currently located in the United States, and will be subject to the laws applicable in the United States. If the database moves to another country, the information in the database may need to be shared in accordance with the laws of that country.

You have a right to refuse this authorization. If you refuse, you will not be able to participate in the screening process for a research study at the Site.

For further information about this authorization or about the VCT database and the privacy policy, please contact the VCT office at 516-998-7499. In the event that VCT assigns all of its rights and/or obligations to an affiliate or a third party in connection with a reorganization, merger, sale of stock or all or substantially all of its assets involving the VCT database, or a similar business combination, it will require the such affiliate or third party to agree in writing to assume and fulfill all of the obligations of VCT under this authorization.

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 Study Doctor at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

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

- By mail: Study Subject Adviser
  Advarra
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00055751.

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.

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.

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. ACKNOWLEDGMENT

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