INFORMED CONSENT FORM
AND
AUTHORIZATION TO DISCLOSE HEALTH INFORMATION

Sponsor / Study Title:	**Cassava Sciences, Inc. / "A Phase 2b, Randomized, Double-blind, Placebo-controlled, Multiple Dose, Biomarker and Safety Study of PTI-125 in Mild-to-Moderate Alzheimer's Disease Patients"**
Protocol Number:	**PTI-125-02**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

This form is for use in a research study that may involve subjects who may or may not have the capacity to consent to take part in the study. When the subject cannot legally consent to take part, pronouns "you" and "your" should be read as referring to the subject rather than the person (legally authorized representative) who is signing and dating this form for the subject. In cases where the subject's representative gives consent, the subject should be informed about the study to the extent possible given his/her understanding. During the course of the study, if the subject regains the capacity to consent, informed consent will be obtained from the subject and the subject offered the ability to leave the study if desired. All subjects will be required to have a caregiver to assist with taking the study drug and other activities.

INTRODUCTION

You are being invited to take part in a research study. You must read, sign and date this form before you agree to take part in this study. This form will give you more information about this study. Please ask as many questions as you need to before you decide if you want to be in the study. You should not sign this form if you have any questions that have not been answered.

The study doctor is being paid by the sponsor (the company paying for this study) to conduct this research study.

You must be honest with the study doctor about your health history or you may harm yourself by participating in this study.

The study drug has previously been given to healthy subjects as a single dose and to a few Alzheimer's disease subjects as a repeated, twice daily oral dose for one month. The study drug was safe and well tolerated in all subjects.

PURPOSE OF THE STUDY

The purpose of this study is to measure changes in cognition and biomarkers following administration of Cassava Sciences, Inc.'s new investigational drug PTI-125 and to determine if there are any side effects associated with the study drug when taken daily for 1 month. PTI-125 is intended to slow the progression of Alzheimer's disease as well as provide some cognitive recovery.

"Investigational" means the study drug being tested is not approved by the United States Food and Drug Administration (FDA) or by any other comparable agency.

A "biomarker" is an indicator that gives information about your health or your response to study treatment.

If you qualify for the study, you will receive PTI-125 or placebo (known throughout this form as the "study drug"). You will receive your dose twice a day for 28 days.

This is a blinded study, which means that neither you nor the study doctor will know whether you will be taking PTI-125 or a placebo. A placebo is an inactive pill, like a sugar pill. Two-thirds of the subjects will receive PTI-125, and one-third will receive placebo. Dependent on further data collected by the sponsor company, you may be eligible for a longer study where everyone will be given PTI-125 active drug.

HOW LONG WILL THE STUDY LAST AND HOW MANY PEOPLE WILL BE IN THE STUDY?

The study will last about 28 days, excluding the screening period. On the first day of dosing, you will stay at the study site for 4 hours after your first dose. You will also be required to make follow-up visits to the study site at least six times during the 28 days. About 60 men and women who have been diagnosed with mild-to-moderate Alzheimer's disease, ages 50 through 85, are expected to be in this study.

WHAT DO I HAVE TO DO TO BE IN THIS STUDY?

You cannot be in this study if you:

- Are in another research study or if you have been in any other research study in which you received study drug within 3 months of your screening visit.
- Have been in the previous study of PTI-125
- Have donated blood within 4 weeks before the first dose of study drug.

<u>Subject Responsibilities:</u>

While participating in this research study, you will need to:

- Be willing and able to follow the study directions and procedures.
- Tell the study staff about any side effects or problems.
- Ask questions as you think of them.
- Tell the study doctor or the study staff if you change your mind about staying in the study.

This study involves testing an investigational drug developed by Cassava Sciences, Inc. (the Sponsor). We ask subjects to keep information as confidential as possible. This would

include not sharing details of the study, including requirements for participation, information received on the risks and benefits of dosing with this study drug, and symptoms or reactions to study drug dosing while enrolled in the study, with persons other than the study staff, your family and your healthcare provider. This would also include not disclosing such information on social media sites or webpages.

WHAT WILL HAPPEN DURING THE STUDY?

Screening

Before the study starts, you will be asked to sign and date this consent form, give your health and social history, and tell study staff if you take any over-the-counter or prescription medicines, vitamins, or herbs.

The study doctor will do some tests to find out if you can be in the study. These tests include:

- Physical exam, including vital signs (blood pressure, temperature, heart and breathing rates), height and weight
- An electrocardiogram (ECG) will be taken - this is a recording of the electrical activity of your heart
- Lab tests (blood and urine)
- Blood test for HIV and hepatitis B and C
- Urine drug screen
- Memory testing – Mini Mental State Exam and Cambridge Cognition testing
- A behavioral/psychological test for suicidal thoughts. If this test is positive, you will be referred for appropriate care
- If you are female and have had your final period less than 24 months ago, or you are uncertain when you had your last period, post-menopausal status will be confirmed by a blood test

The Screening Visit may take up to 2 hours and 30 minutes of your time.

If you meet certain criteria, you will come back for a lumbar puncture for more tests to confirm your diagnosis of Alzheimer's disease. The lumbar puncture sample will also be tested for a neuroinflammation marker (indicating swelling in your brain and/or spinal cord) and possibly other cerebrospinal fluid biomarkers.

- You will have a needle placed in your spine to collect a small amount of cerebrospinal fluid (Lumbar Puncture).
- You will have a test for memory

If you qualify for the study, you will return to the study clinic to start the study. You will stay in the clinic for about two hours. During this time, you will have blood draws, vital signs, and an ECG. You will continue to take study drug each day at home, morning and evening.

You will need to return to the study clinic on the 7th, 14th and 28th days of the study for up to 2 hours. During these two hours the following testing may be performed:

- ECG

- Vital signs
- Listening to your heart and lungs
- Blood draws
- Memory testing

You will return to the clinic once more in the morning of the 28th (last) day of taking the study drug for the same testing along with another lumbar puncture. You will also have a blood draw very close to the time of your lumbar puncture. You will have more memory testing, an ECG and a physical examination.

Study Procedures

Days 1 and study clinic visits

The following will be done before taking the first dose:

- You will be asked questions to be sure that you still qualify for this study.
- You will be asked about any changes in your health or drugs you have taken since your last visit.
- A study doctor or nurse will take your vital signs (blood pressure, heart rate, breathing rate and temperature) and listen to your heart and lungs.
- You will have a test for memory.
- You will have a blood draw for an experimental test to confirm your diagnosis and to measure biomarkers.
- You will have a blood draw for clinical laboratory tests.

After your first dose of Study Drug:

- Standard meals will be given at scheduled times on Day 1 in the study clinic.
- The level of study drug in your blood will be measured on most study clinic visits. About 3/4 teaspoon (4 mL) of blood will be taken.
- Vital signs (temperature, blood pressure, heart rate and breathing rate) will be performed at multiple time points during the study.
- A study doctor or study nurse will listen to your heart and lungs prior to discharge on Day 1 and at every subsequent clinic visit.
- An electrocardiogram (ECG; a recording of the electrical activity of your heart) will be conducted on Day 1 prior to dosing and at all visits except Day 7.
- Lab tests will be conducted (blood and urine) at all visits.
- A blood draw (8 mL) to repeat the experimental test to confirm your diagnosis and to measure blood-based biomarkers (Days 1, and 28).
- You will be monitored for any side effects.
- You will have a behavioral/psychological test, and on Day 28 another test for suicidal thoughts. If this test is positive, you will be referred for appropriate care.
- You will have a blood test for your genotype of the APOE gene. One of these genotypes is linked to a higher risk of Alzheimer's disease. You will not be told the results of this test unless you choose.

If you leave the study early or are withdrawn the following procedures will be performed:

- Vital signs (temperature, blood pressure, heart and breathing rates)

- Physical examination
- Lab tests (blood and urine)
- Electrocardiogram (ECG)
- Memory testing
- Cerebrospinal fluid (CSF) draw

Blood Samples:
Blood samples will be taken by single needle-sticks or by a tube that is left in your arm. You cannot choose how the blood is taken.

There will be about 5 blood draws not including 3 blood draws during screening. The total amount of blood drawn in the study will be about 68 mL, or less than 1/3 of a cup. For comparison, the standard blood donation is about 480 mL (two cups). Additional blood may be drawn and additional tests performed for your safety.

HIV AND HEPATITIS TESTING
As required by the study and if any person is exposed to your blood, you must have your blood tested for the hepatitis viruses and for HIV. HIV is the virus that causes AIDS. If you have a positive HIV or hepatitis test you cannot be in the study.

It may take weeks or months after being infected with HIV for the test to be positive. The HIV test is not always right.

Positive test results may be required to be reported to the State Department of Health. If you have any questions about what information is required to be reported please ask the study doctor or study staff.

Although this testing is supposed to be private, this cannot be guaranteed. For example, it is possible for a court of law to get health or study records without your permission.

Additionally, in the unlikely event that a study employee has been exposed to your blood or other body fluid either through a needle stick injury, splash incident or contact with broken skin (for example, a cut, or a bite), additional samples may be collected to determine and confirm whether or not you have a certain infection. Your de-identified results will be released to the injured employee, and to the health care provider evaluating and treating that employee, to aid the injured employee and the medical provider make decisions regarding his/her medical treatment and follow-up care as a result of this on-the-job exposure.

POSSIBLE SIDE EFFECTS AND RISKS
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 its side effects may not be known. There may be rare and unknown side effects. Some of these may be life threatening.

In pre-clinical (animal studies) the following side effects were seen:

- Vomiting
- Increased salivation
- Increased blood pressure
- Weight loss
- Changes to the size and function of the liver cells
- Seizure

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 staying in this study.

All drugs may cause allergic reactions in some people. Below is a list of symptoms of an allergic reaction:

- Swelling of the face, lips, throat, and other areas of the skin
- Difficulty swallowing or breathing
- Raised, red areas on your skin
- Skin rash, itching, flaking, or peeling

If you have a side effect of the study drug, such as a skin rash or other visible injury, it might be useful to take a digital picture of the affected area to send to the study doctor. By signing and dating this consent, you authorize the study doctor or study staff to take such a picture and provide it to the sponsor. Every effort will be made to protect your identity if a photograph is necessary.

ADDITIONAL RISKS OR DISCOMFORTS

Blood Samples (taken by single needle-sticks or by a tube that is left in your arm):
There may be side effects of having blood drawn such as:

- Fainting
- Redness
- Pain
- Bruising
- Bleeding
- Infection
- Blood clots, which may cause inflammation, swelling and pain
- Nerve damage

If you feel faint, tell the study staff right away.

Risks of Using an Intravenous (IV) Catheter for blood draws:

- Infection
- Pain
- Redness
- Bruising
- Vein irritation from the fluids or medication being given

- Local swelling due to IV fluid (saline) accidentally entering the tissue rather than the vein
- Blood clots, which may cause inflammation, swelling and pain

Spinal Tap or Lumbar Puncture:
Lumbar puncture (spinal tap) is performed in the lower back, in the lumbar region. During lumbar puncture, a needle is inserted between two lumbar bones (vertebrae) to remove a sample of cerebrospinal fluid — the fluid that surrounds your brain and spinal cord to protect them from injury. Side effects may include:

- Headache
- Nausea
- Vomiting
- Dizziness
- Back pain or discomfort which may be significant
- Bleeding at puncture site or rarely into epidural space
- Infection

You will be given a topical anesthetic to reduce pain from the procedure. There are few risks to this anesthetic as it is normally applied, but you may experience mild irritation where the anesthetic is applied and/or numbness in places where the anesthetic may be accidentally applied.

Electrocardiogram (ECG):
The ECG test is a recording of the electrical activity of your heart. The sticky pads used may be cold when applied and sometimes cause some discomfort such as redness or itching. If the hair under the patches needs to be shaved, irritation from shaving also could occur.

Reproductive Risks
Women
Women in this study will not be of childbearing potential.

Privacy Risks
If your data are shared with unauthorized users, you may be at risk of loss of the privacy of your health data. This risk is minimized by protections described in the Confidentiality section below.

Unknown Risks
You might have side effects or discomforts that are not listed in this form. Some side effects may not be known yet. New ones could happen to you. Tell the study doctor or study staff right away if you have any problems.

POSSIBLE BENEFITS OF THE STUDY
This study is short-term, and as such, is not intended to provide medical benefit. However, if the drug appears to benefit subjects, and dependent on further data collected by the sponsor, you may be eligible for a longer study where everyone will be given PTI-125 active drug.

The results of this research study will help guide the development of the study drug and may help others.

ALTERNATIVES TO PARTICIPATING IN THE STUDY
Since this study is for research only, the only other choice would be not to be in the study.

CONFIDENTIALITY
Your records of being in this study will be kept private except when ordered by law. The following people will have access to your study records:

- The investigator
- Sponsor company or research institution [including monitor(s) and auditor(s)]
- The United States Food and Drug Administration (FDA)
- Other state or federal regulatory agencies
- Advarra IRB

The Advarra Institutional Review Board (IRB) and accrediting agencies may inspect and copy your records, which may have your name on them. Therefore, total confidentiality cannot be guaranteed. If the study results are presented at meetings or printed in publications, your name will not be used.

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.

Certificate of Confidentiality
This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the agency which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of, for instance, child abuse or neglect, harm to self or others, and communicable diseases.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

IN CASE OF STUDY RELATED INJURY

If you become ill or are injured while you are in the study, get the medical care that you need right away. You should inform the healthcare professional treating you that you are participating in this study. If you tell the study staff that you think you have been injured then they will help you get the care you need.

If you are injured while in this study, you should contact the study doctor as soon as possible in person or at the telephone number listed on page one of this consent form. Medical care may be obtained in the same way you would ordinarily obtain other medical treatment. If you suffer a study-related injury, the reasonable costs of necessary medical treatment of the injury will be reimbursed by the study sponsor to the extent these costs are not covered by your insurance or other third-party coverage. **No other form of compensation is offered**. A study-related injury is a physical injury that is directly caused by the study drug given as described in the study protocol or by required study procedures that are not standard of care.

To pay medical expenses, the sponsor will need to know some information about you like your name, date of birth, and 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.

Please be aware that some insurance plans may not pay for research-related injuries. You should contact your insurance company for more information.

LEGAL RIGHTS

You will not lose any of your legal rights by signing this consent form, nor will you release the sponsor, study doctor, study staff, or study site from liability.

WHOM TO CONTACT ABOUT THIS 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 IRB
  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: Pro00037146.

PAYMENT FOR BEING IN THE STUDY
You may receive up to $XXXX.00 for being in this study. This money covers the costs for time spent at the clinic and is to help cover travel expenses to and from the clinic. If you choose to leave or are withdrawn by the study staff before finishing all study procedures, you will be paid a lesser amount that is based on the completed visits made to the clinic. If you take study drug, you will be paid as listed below, for each completed visit:

- $XXX.00 for each clinic visit (4 total)

If you successfully complete the entire study, you will receive up to an additional $XXX.00:

- $XXX.00 for completion of entire study (all visits)

You will not be paid for the first screening visit.

No other payment will be offered to you. You will receive your payment within two weeks of your final study visit.

You may be required to report the payment received for this study to the Internal Revenue Service as taxable income.

VOLUNTEERING TO BE IN THE STUDY
It is your choice if you want to be in the study. No one can force you to be in the study. You may not want to be in this study or you may leave the study at any time without penalty or loss of benefits to which you are otherwise entitled. If you break the study rules you may be discontinued from this study.

The study doctor, the sponsor company, Advarra, or the FDA may take you out of the study without your permission, at any time, for the following reasons:

- If you do not follow the study doctor's instructions
- If we find out you should not be in the study
- If the study is stopped
- If it becomes harmful to your health

If you leave the study or if you are taken out of the study, you may be asked to return for a final visit to have some end of study evaluations or tests. If information generated from this

study is published or presented, your identity will not be revealed. If you leave the study, no more information about you will be collected for this study. However, all of the information you gave us before you left the study will still be used.

ADDITIONAL COSTS
There is no cost to you during the study for any of the following:

- Any study test or study procedure, including physical exam and blood tests
- Study drug

NEW FINDINGS
If there is new information or any significant new findings that could relate to your willingness to continue participation, we will tell you. You can then decide if you still want to be in the study.

AGREEMENT TO BE IN THE STUDY
This consent form contains important information to help you decide if you want to be in the study. If you have any questions that are not answered in this consent form, ask one of the study staff.

Please answer **YES** or **NO** to the following questions:

A. Is this document in a language you understand? _____

B. Do you understand the information in this consent form? _____

C. Have you been given enough time to ask questions and talk about the study? _____

D. Have all your questions been answered to your satisfaction? _____

E. Do you think you received enough information about the study? _____

F. Do you volunteer to be in this study of your own free will and without being pressured by the investigator or study staff? _____

G. Do you know that you can leave the study at any time without giving a reason and without affecting your health care? _____

H. Do you know that your health records from this study may be reviewed by the sponsor company and by government authorities? _____

I. Do you know that you cannot be in another study while you are in this study? _____

IF YOU ANSWERED "NO" TO ANY OF THE ABOVE QUESTIONS, OR YOU ARE UNABLE TO ANSWER ANY OF THE ABOVE QUESTIONS, YOU SHOULD NOT SIGN THIS CONSENT FORM.

You will be given a signed and dated copy of this consent form to keep.

_____
Printed Name of Adult Study Subject

_____
Signature of Adult Study Subject Date Time (24-hour clock)

_____
Printed Name of Legally Authorized Representative (if applicable)

_____
Signature of Legally Authorized Representative (if applicable) Date Time (24-hour clock)

_____
Authority of Legally Authorized Representative to act on behalf of Subject (if applicable)

_____
Printed Name of Person Explaining Consent Form

_____
Signature of Person Explaining Consent Form Date Time (24-hour clock)

CAREGIVER ADDENDUM

CAREGIVER PARTICIPATION

As required by the study, every subject must have a caregiver/study partner to participate with them in the study. A caregiver/study partner is a person who spends sufficient time with the study subject so that you can provide certain information. The caregiver/study partner must have the ability to:

- Observe the subject for any changes in health/possible side effects or cognitive function throughout the study.
- Report and assist with the subject's compliance with study procedures and medications.
- Accompany the subject to all study visits and procedures (lumbar puncture).
- Reliably answer interview questions regarding the subject's medical condition, medication use, daily functioning, behaviors, and how he or she feels.

The caregiver/study partner may be compensated for time and travel. As a caregiver/study partner, you will not receive any direct benefit by taking part in this study. Information from this study may also help researchers come up with new tests or medicines in the future to help people with Alzheimer's disease.

Entering a research study is completely voluntary. Although a caregiver/study partner is required for participation, a caregiver/study partner can decide to stop at any time and a replacement will need to be identified. If the caregiver/study partner withdraws from the study, you will only be paid for the study visits completed.

If you have any questions about being a caregiver/study partner in this study, you should ask the study doctor or study staff.

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

If you decide to be in this study, the study doctor and research team will use and share health data about you to conduct the study. Health data may include:

- Your name.
- Address.
- Phone number.
- Date of birth.
- Medical history.
- Information from your study visits, including all test results.

Health data may come from your study records or from existing records kept by your doctor or other health care workers.

For this study, the research team may share health data about you with authorized users. Authorized users may include:

- Representatives of Cassava Sciences, Inc.
- Representatives of Advarra IRB (an Institutional Review Board that reviews this study).
- The Food and Drug Administration (FDA) and other US federal and state agencies.
- Government agencies to whom certain diseases (like HIV, hepatitis, and STDs) must be reported.
- Governmental agencies of other countries.
- Outside individuals and companies, such as laboratories and data storage companies, that work with the researchers and sponsor and need to access your information to conduct this study.
- Other research doctors and medical centers participating in this research, if applicable.
- A data safety monitoring board which oversees this research, if applicable.

Your health data will be used to conduct and oversee the research, including for instance:

- To see if the study drug works and is safe.
- To compare the study drug to other drugs.

- For other research activities related to the study drug.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law and could possibly be used or disclosed in ways other than those listed here.

Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner.

You may revoke (take back) your permission to use and share health data about you at any time by writing to the study doctor at the address listed on the first page of this form. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you decide not to sign this form, you will not be able to take part in the study.

STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing this form.

_____

Printed Name of Adult Subject

_____ _____

Signature of Adult Subject Date Time (24-hour clock)

_____

Printed Name of Legally Authorized Representative

_____	_____	
Signature of Legally Authorized Representative	Date	Time (24-hour clock)

_____

Authority of Legally Authorized Representative to act on behalf of Subject

_____

Printed Name of the Person Obtaining the Authorization

_____	_____	
Signature of the Person Obtaining the Authorization	Date	Time (24-hour clock)