

***Title of research study: Alzheimer's Disease Neuroimaging Initiative 3 (ADNI3) – New Subject ICF***

***Investigator: John Olichney, MD***

***Why am I being invited to take part in a research study?***

We invite you to take part in a research study because you are between the ages of 55 and 90 and fit into one of the three study groups:

- Cognitively Normal (CN) group: participants with no apparent memory problems
- Mild Cognitive Impairment (MCI) group: participants diagnosed with early or late states of mild memory problems
- Mild Alzheimer's disease (AD) group: participants diagnosed with a mild stage AD

You must also have a study partner who is available to accompany you to all study visits for the length of the study.

***What should I know about a research study?***

(Experimental Subject's Bill of Rights)

- Someone will explain this research study to you, including:
  - o The nature and purpose of the research study.
  - o The procedures to be followed.
  - o Any drug or device to be used.
  - o Any common or important discomforts and risks.
  - o Any benefits you might expect.
  - o Other procedures, drugs, or devices that might be helpful, and their risks and benefits compared to this study.
  - o Medical treatment, if any, that is available for complications.
- Whether or not you take part is up to you.
- You can choose without force, fraud, deceit, duress, coercion, or undue influence.
- You can choose not to take part.
- You can agree to take part now and later change your mind.
- Whatever you decide it will not be held against you.
- You can ask all the questions you want before you decide.
- If you agree to take part, you will be given a signed and dated copy of this document.

***Who can I talk to?***

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the study coordinator, Hongzheng Zhang, at 925-357-6914.

For non-emergency issues you can call the UCDMC Hospital Operator (916-734-2011), tell the Operator you are participating in a research study and you wish to talk to the Neurology Resident on call. In the case of an emergency, dial 911 from any phone.

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This research has been reviewed and approved by an Institutional Review Board (“IRB”). Information to help you understand research is on-line at <http://www.research.ucdavis.edu/policiescompliance/irb-admin/>. You may talk to a IRB staff member at (916) 703-9151, [hs-irbadmin@ucdavis.edu](mailto:hs-irbadmin@ucdavis.edu), or 2921 Stockton Blvd, Suite 1400, Room 1429, Sacramento, CA 95817 for any of the following:

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

## ***Why is this research being done?***

This research study will look at the relationship between clinical, cognitive (thinking), imaging, genetic, and biomarker tests in order to understand the full spectrum of Alzheimer’s disease (AD) from its earliest stages. The data from this research study will be used in the development of future research studies that will focus on the treatment of AD at an early stage.

## ***How long will the research last?***

If you are eligible and agree to participate, your participation in this study will last between 3 and 5 years, depending on which study group you fit into.

How often you are asked to come into the clinic during this time will also be based on which study group you fit into:

- CN participants will come into the clinic every other year, with telephone checks occurring on alternating years, for up to 5 years. Some participants in the CN study group will be asked to come into the clinic sooner than every other year for additional PET scans (discussed later in the consent).
- MCI participants will come into the clinic every year for up to 5 years.
- AD participants will come into the clinic every year for 3 years and then will participate in annual telephone checks.

Additionally, CN and MCI participants will take on-line memory tests using home computers every 3 months between clinic visits.

It is possible that additional funding will allow us to extend the study for an additional year. If this occurs, the study team will talk with you about this and you will be asked to sign a separate consent form at that time.

## ***How many people will be studied?***

If you are eligible and agree to participate you will be one of about 1070 - 2000 people enrolled. We will enroll up to 10 new participants at UC Davis. Additionally, 21 people who participated in previous ADNI studies at UC Davis will have the option to join this study, as well. This study is being conducted at about 59 clinical trial sites across the United States and Canada.

This study will continue to follow participants from previous ADNI studies (ADNI-1, ADNI-Go, and ADNI-2) as well as recruit new participants that fit into one of the following 3 study groups:

- Cognitively Normal (CN) group: participants with no apparent memory problems
- Mild Cognitive Impairment (MCI) group: participants diagnosed with early or late states of mild memory problems
- Mild Alzheimer's disease (AD) group: participants diagnosed with a mild stage AD

## ***What happens if I say yes, I want to be in this research?***

***If you are eligible and agree to participate in this study, you will be asked to come into the clinic for an initial Screening Study Visit, a Baseline Study Visit and then return every year or every other year for ongoing Follow-Up Clinic Visits.***

***Depending on which study group you fit into (CN, MCI or AD), there will be between 4 - 6 study visits over the course of the 5 year study. The visits will be completed over multiple days,. Some of the visits will take place in Sacramento, CA. This includes the Magnetic Resonance Imaging (MRI) scan and all of the Positron Emission Tomography (PET) scans. It is possible you will have to go to Sacramento for your Lumbar Puncture (LP), as well, but this is unlikely. All of these procedures are described in detail beginning on page 5 of this form.***

***At the beginning of your screening visit, we will explain all of the study procedures and answer any questions that you and your study partner may have. The screening visit allows the study team to determine if you meet all of the requirements to be in the study, and to make sure it is safe for you to undergo all of the procedures that are required for the study.***

***If you meet the requirements to be in the study, you will be enrolled and move onto the baseline visits. The purpose of the baseline visits are to collect initial results using sample collection (blood and cerebrospinal fluid (CSF)), brain scanning and tests of your memory and daily functioning. The follow-up clinic visits will be used to measure any changes in these results over time.***

***In order to participate in this study, you will need to have an individual (spouse, friend, or relative), called a "Study Partner", who is willing to:***

- ***Accompany you to the study visits, either in person or be available by phone.***
- ***Answer questions about your memory and daily functioning.***
- ***Possibly assist you with logging in to a computer for computer based memory tests.***
- ***Have direct contact with you either in person, by phone or by computer for about 10 hours a week.***

***During this study, Dr. Olichney and his staff will be monitoring your condition.***

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**Description of Study Activities**

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***A table summarizing all study activities will be provided to you and your study partner. Visits may be completed over multiple days. Your study visit schedule may change over the course of the study. A member of the study team will contact you if there are any changes to your study schedule.***

***The following information will be collected at one or more visits over the course of the study:***

- ***At your first clinic visit, we will ask you demographic information (such as how old you are, your occupation, your level of education).***
- ***We will ask about your general medical history and your medical records will be reviewed at the start of the study. At future visits, we will ask you about anything that might have happened during the time between visits, such as changes in your health, any injuries or illnesses, or any reactions to study procedures.***
- ***We will record your height, weight and vital signs (blood pressure, heart rate, breathing rate and temperature).***
- ***We will ask you about any medications that you are currently taking, including any vitamins or supplements.***
- ***You will have a brief physical and neurological exam.***
- ***You will be given written tests of your memory and thinking, and you and your study partner will be asked questions about your daily functioning and your behavior. You can skip any questions you do not want to answer, and you can take breaks if needed.***
- ***If you are in the CN or MCI study groups, you will participate in computer based memory testing, both in the clinic with the study staff and at home on your own. These testing sessions should take about 10-15 minutes to complete.***

***During your clinic visit, you will take the computer based memory tests under the supervision of the study team and then again, 14 days after your clinic visits, from a home computer.***

***You will then repeat the computer based memory test every 3 months in-between clinic visits.***

***If required, a member of the study team will follow up with you by phone to confirm that you have completed the 3-month testing sessions.***

***You can use any computer or device that is connected to the internet and has sound capabilities to take the computer based memory test. You can take the test at your home, at the home of a family member, at the library, etc.***

***If you do not have access to a computer, you will not be able to participate in this part of the study. Please let the study team know if you think you will not be able to participate.***

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- ***If you are in the CN or AD study groups, you will participate in brief telephone checks during the “off” years that you do not come into clinic. For participants in the CN study group, your study partner will participate with you during these phone checks. Study staff will call you and your study partner, and will ask you both about any current medications and vitamins you are taking and any changes in your health that you may have experienced since your last visit. Study staff will also ask your study partner questions about any changes in your behavior or emotional state. These telephone checks should take about 10 – 15 minutes to complete.***

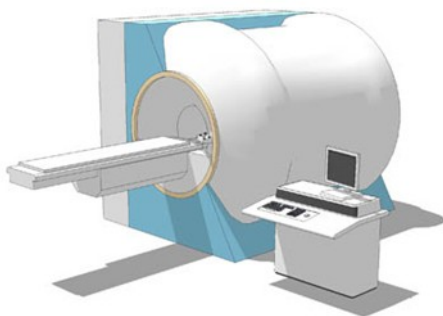
***For participants in the AD study group, a member of the study team will call you annually after you have completed your last in-clinic visit. The purpose of your telephone checks is only to discuss your current wishes with regards to brain donation (discussed later in the consent form) and should only take up 5-10 minutes of your time. If you decide you are not interested in the brain donation program, you will not be called.***

- ***Blood will be drawn from a vein in your arm and a urine sample will be collected for routine laboratory tests that may warn us about any conditions that would make it unsafe for you to undergo this study’s procedures.***
- ***Blood will also be drawn for biomarker and genetic testing, APOE and genome-wide genotyping, DNA and RNA research, and cell line generation. This is described in more detail later in this consent form. You will be asked to fast overnight (a minimum of 6 hours) prior to coming to the clinic for this blood draw. This means no food or drinks such as coffee, tea, milk or juice (water is OK). The total amount of blood that will be drawn from you at each visit will be between 2 and 7 tablespoons.***
- ***You will undergo MRI scans. An MRI uses a large magnet and computer equipment to take electronic pictures of your brain.***

### **MRI Scanner**

***You will lie on your back and enter the MR machine for the scan, during which time you will hear loud knocking noises as the magnet does its work.***

***Each MRI scan will take approximately 45 minutes to complete.***



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- *You will have up to three different types of positron emission tomography (PET) scans as part of the study.*

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- 1) *The first type of PET scan is called an Amyloid PET scan. This type of PET scan uses small amounts of a radioactive imaging agent to measure the amount of beta-amyloid in the brain. Amyloid is a protein that can be associated with the development of AD.*

*The amyloid PET scan in this study will use one of two radioactive imaging agents: either florbetapir or florbetaben. You will be told before the PET scan which imaging agent will be used for your PET scan.*

*The imaging agent will be injected through a vein in your arm. After the injection, you will sit for approximately 50-90 minutes before 20 minutes of scanning. During the scan itself, we will ask that you hold your head as still as possible. The technician will help you find a comfortable position for this.*

- 2) *The second type of PET scan is called an 18F-fluorodeoxyglucose or FDG PET scan. Only participants in the MCI and AD study group will undergo a FDG PET scan and only at the baseline clinic visit.*

*The FDG PET scan uses a very small amount of a radioactive form of sugar to make a picture showing how active your brain is.*

*We will check your blood sugar level before doing this scan. If it is too high we will have to delay the FDG-PET scan.*

*You will be asked to fast for 4 hours before an FDG-PET scan. This means no food or drinks such as coffee, tea, milk or juice (water is Ok).*

*After the FDG is injected you will rest for 30 minutes before a 30-minute scan session, again reducing head movement as much as possible.*

- 3) *The third type of PET scan is called a tau PET scan. The tau PET scan is performed using a radioactive imaging agent called flortaucipir (18F-AV-1451), which we believe sticks to tau protein in the brain. A sticky version of the tau protein builds up in the brains of individuals with AD.*

*Flortaucipir is experimental, which means it has not been approved by the US Food and Drug Administration (FDA) but safety studies have been completed, and the investigators for this study have obtained permission for the use described in this study.*

*Before this tau PET scan is performed, you will undergo an electrocardiogram (ECG). An ECG measures the electrical signals from your heart and is done to make sure there are no safety reason that you should not undergo this type of PET scan. If you have already undergone an ECG within the last 12 months, you may be able to skip this ECG.*

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***Flortaucipir will be injected through a vein in your arm. You will rest for about 75 minutes after the injection, before lying in the PET scanner for a 30 minute scanning session. As with the previous types of PET scans, we will ask that you reduce head movement as much as possible.***

***After the scan is finished, you will be asked to drink fluids before leaving the scan facility to help empty your bladder and to continue to drink fluids at home to wash the remaining imaging agents from your system.***

***A member of the study team will call you approximately 2-3 days after this tau PET scan to see how you are feeling.***



- Right before each PET scan begins, you will undergo computerized x-ray (CT scan). The CT scan uses X-rays to take a picture of your brain (including bones) to help align the position of your head before each PET scan.
- A lumbar puncture (LP) will be performed. A lumbar puncture is a procedure that involves inserting a needle in the lower back, below the spinal cord, in order to collect a small amount of the spinal fluid that washes around the brain and spinal cord, called cerebrospinal fluid (CSF).

During the procedure you will lie on your side curled up into a ball or you will sit on the edge of a chair or bed and lean forward.

You will be asked to fast overnight (a minimum of 6 hours) prior to coming to the clinic for the LP. This means no food or drinks such as coffee, tea, milk or juice (water is OK).

The lower part of your back will be cleaned with antiseptic. A local anesthetic will be injected into the skin of your lower back at the area of the lumbar puncture.

When the area is numb, a very thin needle will be inserted into the spinal canal in the lower back, well below the level where the spinal cord ends. About 20 milliliters (mLs), less than 1½ tablespoons, of spinal fluid will be removed for analysis and storage. Your body replaces this spinal fluid within 2 hours.

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After the lumbar puncture is completed, you will remain in the clinic for about 30 minutes. You will be given something to eat and drink before you leave.

***You should avoid any strenuous physical activity for the next 24 hours. This includes lifting, bending, doing housework and gardening, or doing exercise such as jogging or bicycle riding.***

***Study staff will call you the day following your lumbar puncture to discuss how you are feeling.***

## Random Selection of Additional Tau PET scan visits

A percentage of participants in the CN and MCI study groups will be randomly selected to undergo 2 additional tau PET scans. This randomization will not occur until after you have completed your Baseline clinic visit. If you are selected to come into the clinic for these additional tau PET scans and are not already scheduled for a full follow-up clinic visit, we will also ask that you complete a follow-up clinic visit at that time as well.

A member of the study team will contact you after your Baseline visit to let you know if you have been selected to undergo the additional tau PET scans and will let you know your updated visit schedule.

## Genetic & Biomarker Research

During this study, your samples will be used to extract genetic material, including DNA and RNA, to grow cell lines, for genomic testing and for biomarker research.

### **Genetic Research**

The cells of your body contain deoxyribonucleic acid or “DNA” for short. DNA carries the code for the genes that determine your physical appearance such as the color of your hair and eyes. Genes in your DNA that are active lead to higher levels of ribonucleic acid stretches or “RNA” for short. RNA levels from your cells can be measured to study the activity of genes. DNA and RNA will be extracted from your blood samples for genetic research related to AD and aging.

Genomic studies will be done. This means that researchers will look at your complete set of DNA, including all of your genes. You will not be told the results of any of your genomic testing.

The results of these genetic and biomarkers tests will be maintained in scientific databases for this research study. These results are important only for research - not for helping care for you. For this reason, the results will not be released to you or your family.

No information regarding your genetic or biomarker tests results will be entered into your regular medical record. If you are concerned about a potential genetic disorder, you should discuss this with your primary care doctor. You and your doctor may choose to test specifically for it, but this would require separate blood samples and would not be part of this research study.

## Biomarker Research

A biomarker is a specific physical trait used to measure the progress of a disease or condition. We will look at biomarkers in your blood and CSF to learn how they may be related to the progression of memory problems.

## Immortalized Cell Line

Cell lines provide a living, growing source from which genetic material (ex: DNA and RNA) can be continually extracted. This means that blood cells will be grown and maintained in the laboratory which will allow researchers to continue to study your genes for many years. Please discuss any concerns about this process with study staff before signing this consent form.

## Sample Storage & Future Use

Your samples (blood, CSF, and cell lines) will be sent to the laboratories at the National Cell Repository for Alzheimer's Disease (NCRAD) at Indiana University and at the University of Pennsylvania.

Your samples will be maintained in these laboratories for many years. These samples will be coded and will not be identified by your name or any other personal identifiable information. These de-identified samples are necessary for long-term research and will be stored indefinitely.

Your samples may be provided to researchers at academic institutions, hospitals, and biotechnology/pharmaceutical companies studying various diseases including AD and aging. Successful research using your samples could result in commercial or therapeutic projects with significant value, such as a product for the medical treatment of Alzheimer's disease or for diagnosing a mutation responsible for the disease. You will not share in any financial benefits of these uses.

## What will happen to my research data?

All of the data collected in this study including your clinical data, neuropsychological test data, MRI and PET scans, biomarker and genetics data will be sent to the Laboratory of Neuro Imaging (LONI) at the University of Southern California (USC) where they will be stored indefinitely and shared for future research.

Your privacy will be protected. Your data will be labeled with a coded research identifier to protect your identity. Your name and other information which identifies you will not be linked to your research data.

All of the research data will be made available to qualified investigators at other scientific institutions around the world for research purposes.

Because this study is supported by the National Institutes of Health (NIH), de-identified genetic data will be submitted to government health research databases for broad sharing with approved researchers. Broad sharing of research data will assist other researchers

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investigating various diseases, including Alzheimer's disease and dementia. All data will be de-identified, so it will not be possible to tell who you are from the data that is submitted. Upon request, your data may be withdrawn at any time. However, data that has already been distributed for approved research prior to the date of your withdrawal cannot be retrieved.

## Federal Interagency Traumatic Brain Injury Research (FITBIR) Data Sharing (Optional)

The Department of Defense (DOD) has funded a portion of the tau PET scans being conducted in this study. The tau imaging data from ADNI3 participants will be compared with tau imaging data from another study designed to look at the relationship between Post Traumatic Stress Disorder (PTSD) and Traumatic Brain Injury (TBI) and the development of AD. Because of this, coded Tau PET imaging data from consenting participants will be shared with the Federal Interagency Traumatic Brain Injury Research (FITBIR) Informatics System. FITBIR is a central repository and resource for sharing data that was developed by the Department of Defense and the National Institutes of Health (NIH) to promote collaboration, accelerate research, and advance knowledge on the characterization, prevention, diagnosis and treatment of TBI. All data are coded, and identities will not be disclosed to the FITBIR Informatics System. You do not have to agree to have your data uploaded to FITBIR to participate in the ADNI3 study.

## Global Unique Identifier (GUID)

Each participant in ADNI3 will receive a Global Unique Identifier (GUID). A GUID is a computer-generated alphanumeric code that is unique to each research participant.

In order to generate the GUID, study staff will enter 4 pieces of your personal information into a "GUID generator", your birth name, birth date, gender and city of birth, which will be used to generate a unique code. This code will be sent to LONI where the GUID will be assigned and stored along with ADNI study data.

## Brain Donation Program

Much can be learned about the human brain by studying it under a microscope. This detailed examination of the brain after death is essential in determining the true causes of dementia. Brain tissue is necessary for diagnosis and for helping research into the causes and better treatment of Alzheimer's disease. With permission, the findings from this examination will be shared with his or her next of kin. Therefore, we are asking each participant in this study if they are interested in taking part in the brain donation program for research (autopsy) at time of death. If you want to take part in this program, you will be asked to sign a separate Brain Donation consent form.

You can decline and still participate in this study, and you can change your mind at any time.

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

If you take part in this research, you will be responsible to:

- Report all injuries, illness or reactions to study procedures to the study staff so that it can be recorded in your study records.
- Follow the instructions you are given.

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- Come to the study site for all visits.
- Tell the study staff about any changes in your health.
- Tell the study doctor about all medications you are taking and check with the study doctor before you begin taking a new medication.
- Tell the study doctor or study staff if you want to stop being in the study at any time.

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

You may decide not to take part in the research and it will not be held against you.

This is not a treatment study. The alternative to participating in this study is to not participate.

Starting a new medication at any point during the course of the study should be discussed with your study doctor.

## ***What happens if I say yes, but I change my mind later?***

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

In the event that you end your participation in the study early, you will be asked to return to the clinic site to undergo a final evaluation. This will include all of the procedures normally performed at a follow-up clinic visit.

You may also decide that you no longer want to participate in follow-up clinic visits, and decide that you want to continue to be followed by annual telephone checks only. If this occurs, you will be asked to sign a separate consent form.

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

There are known and possibly unknown risks associated with this study. You might experience all, some, or none of the side effects listed below. Let Dr. Olichney know if you experience any side effects. You will be told of any new risks or significant findings that develop during the course of this study.

### Risks of Blood Draws

Removal of blood by a needle and syringe poses a small risk of infection or temporary pain or bruising at the site of the needle stick. Some people may experience fainting or dizziness. To minimize these risks, experienced medical personnel will handle all the blood drawing procedures and sterile conditions will be maintained.

In total, up to 460 mLs of blood (about 31 tablespoons) may be taken over the course of this study. The exact amount will depend on the number of clinic visits your study group will participate in during the course of the study. Your body will make up for this loss.

### Risks of Lumbar Punctures

In total, up to 60 mLs (a little more than 4 tablespoons) of CSF may be collected over the course of the study. The exact amount will depend on the number of lumbar punctures your study group will undergo during the course of the study. Your body will make up for this loss.

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During the lumbar puncture procedure, you may have temporary pain and discomfort in your back.

Headache may occur in about 5% of people who undergo a lumbar puncture. Less commonly, in about 1 - 4% of participants, a persistent low-pressure headache may develop, probably due to leakage of CSF. If this headache persists it may require additional treatment. Uncommonly, a blood patch (injection of some of your blood into the lumbar puncture site to patch the CSF leak) may be required and should relieve the headache immediately.

Although very rare, it is possible that you may have an allergic reaction to the local anesthetic, like lidocaine, used for the lumbar puncture. An allergic reaction would cause swelling and a rash on your skin where the anesthetic was injected. Please alert the study staff if you have ever had a reaction to local anesthetic before (especially if this occurred with a dental procedure).

Potential but rare risks of lumbar puncture include infection, damage to nerves in your back, and bleeding into the CSF space. The risk of these event occurring is much less than 1%. To minimize these risks, the lumbar puncture will be performed by Dr. Olichney or by a specialist specifically trained in the procedure.

## Risks of MRI Scans

An MRI may cause possible discomfort for people due to the loud knocking sounds made by the machine and the confined space of the testing area. There is also a risk of injury if metal is brought into the imaging room, which might be pulled into the MRI magnet.

People with pacemakers, aneurysm clips, artificial heart valves, ear implants or metal/foreign objects or implants are not permitted to have an MRI.

## Risks of PET Scans

The primary risk of PET scans is radiation exposure. This radiation is necessary to create the images. This radiation exposure is not necessary for your medical care and is for research purposes only. This study involves a radiation exposure that is typical of other diagnostic tests involving radiation exposure. The amount of radiation exposure received in this study is below the levels that are thought to result in a significant risk of harmful effects.

Other risks associated with PET scanning include fatigue and discomfort at having to remain in the scanner for up to 30 minutes, and the discomfort and possible bruising associated with intravenous injections.

To minimize these risks, this study uses the lowest possible dose of radioactivity needed to obtain a clear image. All IV catheters are placed by medical professionals with extensive training and experience. If you experience anxiety or discomfort at any time while in the PET scanner, you can communicate via intercom with the technician at any time during the scan.



## Risks of $^{18}\text{F}$ -FDG PET Scan

FDG is considered safe and there has not been a report of an adverse event (side effect) with this type of PET scan. Despite this information there is still a possibility of a rare allergic reaction.

## Risks of Amyloid PET Scans: Florbetapir and Florbetaben

The most common side effects reported in studies using florbetapir lasted only a short time and included: headache, muscle or bone pain, increased blood pressure, nausea, fatigue, injection site reaction (bleeding, irritation, pain), anxiety, back pain, claustrophobia (fear of being in closed or narrow spaces), dizziness, feeling cold, insomnia (inability to sleep) and neck pain. Less common side effects reported were: infusion site rash, altered taste in the mouth, itchiness, rash (hives), and flushing, but participants never experienced all of these side effects simultaneously.

The most common side effects reported in studies using florbetaben were injection site reactions consisting of erythema (redness of the skin), irritation and pain.

## Risks of Flortaucipir ( $^{18}\text{F}$ -AV-1451) PET Scan

The following side effects have been reported in clinical studies: diarrhea, headache, and altered taste. All reported events were mild in intensity and all subjects recovered from these events. Since flortaucipir ( $^{18}\text{F}$ -AV-1451) is a new compound that is being studied in clinical trials, you may experience side effects that we do not know about yet.

No long-term animal studies to study the risk of cancer from AV-1451 have been done. The non-radioactive version of AV-1451 has been tested in bacteria and short-term animal studies to study the risk of cancer. In laboratory tests with bacteria cells, AV-1451 showed positive results for genotoxicity (damage to genes). Damage to genes can lead to the development of cancer. However, other studies done in living animals with AV-1451 at doses over 750 times the highest human dose did not show any evidence for damage to genes.

A 14-day follow-up single dose toxicity study in rats seemed safe with no drug-associated risks at doses that were up to 150 times the intended maximum human dose. A month long repeat dose toxicity study in rats and dogs seemed safe with no drug associated risks at doses that were up to 50 times the intended maximum human dose. Since the drug is still under development, there may be risks that are still unknown.

At this time the effects of flortaucipir ( $^{18}\text{F}$ -AV-1451) to a developing fetus are not known. It is however known that higher levels of radiation, above what you would be exposed to during this study, can cause damage to a developing fetus.

Women of child-bearing potential cannot participate this study.

## Risks of Testing & Questionnaires

Memory and cognitive testing may cause some individuals to become upset, frustrated, or

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tired. You have the right to decline to answer any questions that you feel uncomfortable in answering. You may ask to stop testing at any time for any reason.

## Risks of Genetic Testing

Under some circumstances, it can be a risk for genetic information to be known by others. Variation in some genes is known to be directly related to risk of certain illnesses. In some cases, knowledge of genetic information could have negative psychological consequences or could affect access to or retention of certain benefits or entitlements. For example, the information could potentially be used against subjects if it were revealed to insurance companies or potential employers.

Although your genetic information is unique to you, you do share some genetic information with your children, parents, brothers, sisters, other blood relatives and other members of your ethnic group. Consequently, it may be possible that genetic information from you could be used to help identify them. While information traditionally used to identify you will not be released (i.e. name, date of birth, address, telephone number), people may develop ways in the future that would allow someone to link your genetic or medical information back to you. A U.S. Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally prohibits health insurers or health plan administrators from requesting or requiring genetic information of an individual or an individual's family members, or using such information for decisions regarding coverage, rates, or preexisting conditions.

GINA also prohibits employers from using genetic information for hiring, firing, or promotion decisions, and for any decisions regarding terms of employment. You should be aware, though, that if your genetic information were accidentally released to the wrong source, federal law does not protect against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance or by adoption agencies. You will not learn the results of the genetic portion of the study nor will the results be made available in your medical record. Furthermore, the researchers have adopted strict privacy and confidentiality procedures for maintaining your genetic information as described in this consent form.

## Risk of Loss of Confidentiality

All of the de-identified data collected in this study will be shared broadly. There is a slight risk that there could be a breach in the security of research database systems resulting in the access of information. Safeguards are in place to minimize this risk.

## ***Will being in this study help me in any way?***

We cannot promise any benefits to you or others from your taking part in this research. However, you will receive close monitoring and follow-up of your health during your time in this study. We also hope that the knowledge gained will be beneficial to society in improving our understanding of risk for cognitive decline in older individuals.

## ***What happens to the information collected for the research?***

Efforts will be made to limit use or disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot

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promise complete confidentiality. Organizations that may inspect and copy your information include the IRB and other University of California representatives responsible for the management or oversight of this study; the Study Sponsors, National Institute on Aging (NIA) and Northern California Institute for Research and Education (NCIRE) and its representatives; Alzheimer's Therapeutic Research Institute (ATRI) at the University of Southern California (USC) who is the coordinating center for this study and those working with ATRI to conduct this research study; Department of Defense (DOD); Laboratory of Neuro Imaging (LONI) at USC; Other research sites participating in this study; Data and Safety Monitoring Board (DSMB) and the study monitors who oversee the safety of this study; Laboratories used for this study; Government regulatory agencies (such as the FDA and the Office for Human Research Protections (OHRP)).

The sponsor, monitors, auditors, the IRB, the Food and Drug Administration will be granted direct access to your research records to conduct and oversee the study. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

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

If we access protected health information (e.g., your medical record), you will be asked to sign a separate form to give your permission. Your medical records may become part of the research record. If that happens, your research records may be looked at by the sponsor of this study and government agencies or other groups associated with the study.

Federal law provides additional protections of your medical records and related health information. These are described in the UC Davis Health System Notice of Privacy Practices (<http://www.ucdmc.ucdavis.edu/compliance/pdf/notice.pdf>) and in an attached document.

Certificate of Confidentiality from the Federal government that will help protect the privacy of the research records. The Certificate of Confidentiality allows the Researchers to refuse to disclose identifying information on your participation in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level.

A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself and your involvement in this research. If you have given your consent for an insurer or employer to obtain information about you, the Researcher may not use the Certificate of Confidentiality to withhold this information. A Certificate of Confidentiality also does not prevent a Researcher from disclosing information about you to prevent serious harm to yourself or others, such as reporting to the authorities' incidents of child abuse, elder abuse or spousal abuse.

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***What happens if I am injured as a result of taking part in this research study?***

All forms of medical findings and treatments – whether routine or experimental – involve some risk of injury. In spite of all safety measures, you might develop medical problems from participating in this study.

It is important that you promptly tell the person in charge of the research if you believe that you have been injured because of taking part in this study. If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. Depending on the circumstances, the costs of the treatment may be covered by University or may be billed to your insurance company just like other medical costs. The University does not normally provide any other form of compensation for injury. The NIA, NCIRE and ATRI do not provide compensation for research-related injury. For more information about compensation, you may call the IRB Administration at (916) 703-9151 or email at [HS-IRBAdmin@ucdavis.edu](mailto:HS-IRBAdmin@ucdavis.edu).

***Can I be removed from the research without my OK?***

The person in charge of the research study or the sponsor can remove you from the research study without your approval. For instance, if you consistently fail to participate in clinical follow-up evaluations, you may be removed from the study.

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

***What else do I need to know?***

This research is being funded by Northern California Institute for Research and Education (NCIRE) with the Alzheimer's Therapeutic Research Institute (ATRI). It is funded by a grant from the National Institute on Aging (NIA).

UC Davis is being paid to conduct this study, but the study doctor and research staff have not received any direct income from the sponsor.

There is no charge for you to participate in this study. Neither you nor your insurance carrier will be charged for your taking part in the research. All costs associated with the study will be paid by the sponsor/department.

In return for your effort and travel expenses, you will be paid \$50 for each clinic visit you complete. In addition, you will be paid \$50.00 for each MRI, \$100.00 for each PET scan, and \$200.00 for each LP. You will be paid in the form of a check mailed to your home within 45 days of completing all study procedures for that year, as required by your particular study group (CN, MCI, or AD).

***Is participation in this research study voluntary?***

Your participation in this research study is entirely voluntary. You have the right to refuse to participate. You may discontinue participation in this study at any time without jeopardy to the medical care you receive at this institution.

You have the right to not sign this form that allows us to use and share your health information for research; however, if you don't sign it, you cannot take part in this research study.

You have the right to withdraw your permission to use or disclose personal information about your health and the future use of your samples.

If you choose to withdraw your permission and/or future use of samples, you must notify Dr. Olichney in writing.

Dr. Olichney's mailing address is:  
John Olichney, MD  
UC Davis Department of Neurology  
4860 Y Street, Suite 3900  
Sacramento, CA 95817

Dr. Olichney will still be able to use the information collected about you prior to your withdrawal from the study. Information and samples that have already been shared with researchers cannot be withdrawn.

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## STATEMENT OF CONSENT

By signing this page, you are confirming the following:

- You have read all of the information in this consent form, and you have had time to think about it.
- All of your questions have been answered to your satisfaction.
- You voluntarily agree to be part of this research study, to follow the study procedures, and to provide necessary information to the study doctor, nurses, or other staff members, as requested.
- You may freely choose to stop being a part of this study at any time.
- You allow the study doctor and the sponsor to use and disclose your personal health information as described in this document.

You will receive a copy of this signed consent form to keep.

By signing this consent you are authorizing the use of your data and biological materials for large scale, multi-center studies that will combine data from similar populations. These multi-center studies are being conducting by the Alzheimer's Disease Neuroimaging Initiative (ADNI), a neuroscience consortium of universities and research institutions. Your data and biological samples will be stored with a coded research identifier to protect your identity. Only de-identified data, which does not include anything that might directly identify you, will be shared with ADNI members and the general scientific community for research purposes. This data will be entered into study databases to be used from this date and going forward. Genetic data may be made available on NIH-approved secure databases.

### Contact for Future Studies

As we continue to learn more about genetic markers and biomarkers, we would like your permission to contact you about possible future biomarker, genetic and family studies. May we contact you about future studies?

- ☐ **Yes**, you may contact me about future studies.
- ☐ **No**, you may not contact me about future studies.

### FITBIR Data Sharing

Do you agree that your Tau PET imaging data may be uploaded to the FITBIR database?

- ☐ **Yes**, my Tau PET imaging data may be uploaded.
- ☐ **No**, my Tau PET imaging data may not be uploaded.

### Brain Donation Program

Are you are interested in considering brain autopsy after death? You will be asked to sign a separate Autopsy consent form in the future.

- ☐ **Yes**, I am interested in brain donation
- ☐ **No**, I am not interested in brain donation

**By signing below, you voluntarily agree to participate.**

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## Signature Block for Capable Adult

Your signature documents your permission to take part in this research.

\_\_\_\_\_  
Signature of subject

\_\_\_\_\_  
Date

\_\_\_\_\_  
Printed name of subject

\_\_\_\_\_  
Signature of person obtaining consent

\_\_\_\_\_  
Date

\_\_\_\_\_  
Printed name of person obtaining consent

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

\_\_\_\_\_  
Signature of witness to consent process

\_\_\_\_\_  
Date

\_\_\_\_\_  
Printed name of person witnessing consent process

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**Signature Block for Adult Unable to Consent**

Your signature documents your permission for the named subject to take part in this research.

\_\_\_\_\_  
Printed name of subject

\_\_\_\_\_  
Signature of legally authorized representative

\_\_\_\_\_  
Date

\_\_\_\_\_  
Printed name of legally authorized representative

\_\_\_\_\_  
Signature of person obtaining consent

\_\_\_\_\_  
Date

\_\_\_\_\_  
Printed name of person obtaining consent

Assent ☐ Obtained  
☐ Not obtained because the capability of the subject is so limited that the subject cannot reasonably be consulted.

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

\_\_\_\_\_  
Signature of witness to consent process

\_\_\_\_\_  
Date

\_\_\_\_\_  
Printed name of person witnessing consent process

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## STUDY PARTNER INFORMATION & CONSENT

As the subject's study partner, you have important tasks that need to be carried out in order for the study to be conducted in the safest and best manner possible. These responsibilities include:

- 1) You must have direct contact with the participant at least one day (a minimum average of 10 hours) per week.
- 2) You must be able to accompany the participant to all clinic visits, or be available via phone to answer questions from study staff.
- 3) You will be asked general questions about yourself (such as age and gender) as well as about your relationship to the participant. You also will be asked questions about the participant's health, memory, thinking, function and emotional well-being in order to learn about any changes in the participant.

If for any reason you become unable to carry out your responsibilities, please tell the study team immediately. You may be asked, if possible, to select a substitute who can take over your duties.

You have read all the preceding information which describes both the subject's participation in the study and your involvement as the subject's study partner. The study has been explained to you in detail. All your questions have been answered to your satisfaction.

You voluntarily agree to participate as a Study Partner.

☐ YES

☐ NO

\_\_\_\_\_ Study Partner's Initials

\_\_\_\_\_  
Study Partner's Name (print)

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Person Obtaining Consent  
(print)

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

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