UNIVERSITY OF CALIFORNIA, SAN FRANCISCO CONSENT TO PARTICIPATE IN A RESEARCH STUDY

STUDY TITLE: Veri-T: A Phase 1, Randomized, Double-Blind, Placebo-Controlled, Safety, Tolerability, Pharmacokinetics, Pharmacodynamics and Preliminary Efficacy Study of Oral Verdiperstat (BHV-3241) in Patients With Semantic Variant Primary Progressive Aphasia (svPPA) Due to Frontotemporal Lobar Degeneration With TDP-43 Pathology (FTLD-TDP)

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We are asking you to consider taking part in a research study being done by Peter Ljubenkov, M.D. from the UCSF Department of Neurology. The first part of this consent form gives you a summary of this study. We will give you more details about the study later in this form. The study team will also explain the study to you and answer any questions you have.

Research studies include on people who choose to take part. It is your choice whether or not you want to take part. It is your choice whether you want to take part in this study. Please take your time to make a decision about participating. You can discuss your decision with your family, friends, and health care team.

If you are the legally authorized representative, the person you are representing (hereafter referred to as "you") is being asked to participate in a research study but is unable to consider whether to give consent to participate because of their medical condition. You, as the subject's legally accepted representative, are being asked to consider whether to give consent for the subject to participate in this study.

Why is this study being done?

The researchers want to find out what effects, good and/or bad, an experimental drug called Verdiperstat (also known as BHV-3241), has on you and your Semantic Variant Primary Progressive Aphasia (svPPA) due to Frontotemporal Lobar Degeneration with TDP-43 Pathology (FTLD-TDP). This is the first time Verdiperstat has been given to patients with svPPA due to FTLD-TDP.

The study will also test the effects of Verdiperstat on your cerebrospinal fluid (CSF) and blood proteins, brain magnetic resonance imaging (MRI), activity levels, and cognitive (thinking and memory) function.

The study is funded by the National Institutes of Health (NIH) and Part the Cloud, Alzheimer's Association. The study drug is paid for by the manufacturer, Biohaven Pharmaceuticals, Inc.

How many people will take part in this study?

A total of approximately 64 subjects between the ages of 18 and 85 years of age are expected to enter the study.

What will happen if I take part in this research study?

If you choose to take part in the study, you will be asked to take the study drug or a placebo (a pill that looks like the study drug but has no drug in it) for 24 weeks. You will be in the study about 8 months and visit the research center about 12 times. Your total time commitment during the study is approximately 51.5 hours.

Your study doctor or nurse will make sure you know when you need to come for study visits. You will be asked to come to each visit with a study partner. Your study partner is someone who knows you well and will verify information gathered at research visits. It is important that you have the same study partner who comes with you each time to each study visit. **At the end of this consent form is a table that show what will happen to you at each of the study visits if you participate.*

Most study visits will take place at the:

- Neurosciences Clinical Research Unit (NCRU) and Neuroscience Imaging Center (NIC), at 675 Nelson Rising Lane, San Francisco, CA 94158, UCSF Mission Bay Campus

But optional CT-guided lumbar puncture visits may take place at the:

- UCSF Imaging Center at China Basin, 185 Berry Street, Lobby 6, San Francisco, CA 94107

To determine if you are eligible for the study:

Following is a more complete description of this study. Please read the description carefully. You can ask questions you want to help you decide whether to join the study. If you join the study, we will give you a signed copy of this form to keep for future reference.

First, you will first complete a screening period that will last up to 6 weeks. During this time, you will need to have the following exams, tests or procedures done so that the study doctor can find

out if you can be in the main part of the study. Screening procedures may take place over several days, if necessary. The initial screening visit includes the following:

- **Medical history review:** Your study doctor will ask questions about the medications, herbs and supplements you have taken in the last few months and are still taking, about your svPPA due to FTLD-TPD, your medical history, including your smoking history, and your surgical history. You will be asked if you are able to swallow pills whole because the study drug may not be crushed or chewed.
  - **Measurement of your vital signs:** Your blood pressure, pulse, respiratory rate, and temperature will be measured after resting for 5 minutes. Your blood pressure and heart rate will be taken while you are lying down and standing.
  - **Physical and neurological examination:** You will have a physical examination, similar to those done for regular medical care, and a neurological examination. Your height and weight will be recorded.
- **Electrocardiogram (ECG):** A 12-lead electrocardiogram will be performed. This is a painless procedure that measures electrical activity of your heart.
- **Blood drawing (venipuncture)**: At the screening visit you will be asked to give a blood sample for routine hematology, hemoglobin A1C (a simple blood test to measure average blood sugar level over past few months), chemistry including kidney function tests, liver function tests, thyroid function tests, uric acid tests (uric acid is a normal waste product that's made when the body breaks down certain substances found in your own cells and also in some foods.), and coagulation (blood clotting) laboratory tests by having a needle inserted into a vein in your arm.

  Approximately 2 Tablespoons (30mL) of blood will be drawn at the screening visit. The total amount of blood collected over the entire study duration of the study is approximately 316 milliliters, which is about the same as 21 Tablespoons, which is less than the amount of blood that you would give for one (1) voluntary blood donation (a blood donation is approximately 450mL).
- **Urine sample:** You will be asked to give a urine sample for a routine urine test.
- **Pregnancy testing (female subjects):** If you are a woman of childbearing potential a serum pregnancy test (blood test) will be performed to confirm you are not pregnant at screening.
- **Cognitive and functioning testing:** Thinking and activities of daily living (ADLs) questionnaires will be given and it may take up to 30 minutes for you to complete. Some of the cognitive testing will be completed by paper and pencil, and some using a mobile device application. The study staff will explain how to use the mobile device.
- **Well-being questionnaire:** You will be asked to complete a questionnaire about how you are feeling emotionally.

- **Optional demographics questions:** the study staff will give you an optional demographics form with questions about how you identify and describe yourself. This form will help the study team understand more about who takes part in clinical trials. You can choose to answer these questions, or you can choose not to answer them. Your eligibility to participate in this clinical trial will not be affected by your decision to complete the form or not, and your eligibility will not be affected by any answers to these questions.
    - ☐ **I agree to participate in the optional demographics questions.**
    - ☐ **I do not agree to participate in the optional demographics questions.**

If the screening exams, tests and procedures show that you can continue to be in the study, and you choose to take part, you will have the following additional screening tests and procedures done before the Day 1 Visit (first study drug dosing):

- **MRI scan procedure:** Once you have completed the screening visit and the study doctor determines that you seem to meet the study entrance requirements, you will be scheduled for a brain MRI scan. The MRI scan will produce pictures of your brain for the study doctors to review. For the MRI scan, you will lie down on a narrow bed, which will then be placed in a tunnel that is 6 feet long by 22 inches wide and open at each end. You will need to lie there quietly for about 45 minutes to one hour, during which time there will be a loud banging noise. An MRI does not involve any radiation exposure and is painless. If the images from the MRI are not of the required quality, you may be asked to come back to the MRI scan center for another MRI scan on another date. The MRI brain scan will only be done if you meet all other eligibility requirements after completing the above screening procedures.
- **Lumbar puncture (spinal tap):** If you continue to meet the study entrance requirements after completing the MRI, you will have a lumbar puncture to collect cerebrospinal fluid (CSF) from your spine. A lumbar puncture (LP) for collection of CSF will be performed 2 times during the study, once at screening and once at the end of the 24 week treatment period (or at the early termination [ET] visit if you do not complete the entire 24 week treatment period).
    - You will need to stop taking any anti-inflammatory medications and aspirin 5 days prior to each lumbar puncture.
        - A lumbar puncture requires that you either sit or lie with your knees drawn up to your stomach. The study doctor will first inject a medication (local anesthetic) to numb an area of your lower back. The study doctor will then insert a hollow needle into the spinal fluid sac at the base of your spine and draw out approximately 1 ½ Tablespoons of spinal fluid. You will need to remain very still to avoid moving the needle. This procedure takes about 15 minutes. You will be required to remain in bed for approximately one hour following the procedure.
        - The CSF will be tested for chemicals or proteins that may be associated with the presence of neurodegenerative disease, such as tau and neurofilament proteins. Additionally, routine laboratory measures normally done during a lumbar puncture (LP) (for example lab tests measure cell count, protein, and glucose level) could

indicate potential inflammation and help us learn more about the treatment of neurodegenerative brain conditions.

- You or your study partner will be contacted by telephone approximately 24 hours after the lumbar puncture procedure to see how you feel.

- **(Optional) Computerized Tomography (CT)-guided lumbar puncture**: A CT-guided lumbar puncture is available, if deemed necessary by the principal investigator. A CT- guided lumbar puncture combines a series of imaging scans from several angles with computer processing to re-create three-dimensional images of the anatomical structure of your spine. Using CT scans as a guide will allow the doctor to maximize precision in accessing the cerebral spinal fluid (CSF). Once the CT scan is performed, the doctor will insert the needle with the help of the CT scan images and perform the lumbar puncture.

After you complete all of the screening procedures, the study doctor will confirm whether or not you are suitable for participation in the study. There are several reasons that you may not be eligible to participate in the study. Your study doctor can discuss these reasons with you. For instance, you may not be able to be in the study if you have recently changed or started any new medications, or if you have had a history of specific illnesses in the past.

During the main part of the study:

If the screening exams, tests and procedures show that you can continue to be in the study, and you choose to take part, you will return to the research center to have the following tests and procedures done:

Baseline Day 1 Visit (First Study Drug Administration). This visit may take up to 7 hours to complete.

Pre-dose on Day 1: Before the first dose is given you will have the following:

- **Symptom and medication review:** At every study visit you will be asked how you are feeling and whether you have had any problems since the last visit. You will also be asked about any changes in your medications, vitamins or other supplements. You must be able to swallow study drug pills whole because the study drug may not be crushed or chewed.
- **Measurement of your vital signs:** Your blood pressure, pulse, respiratory rate, and temperature will be measured after resting for 5 minutes. Your blood pressure and heart rate will be taken while you are lying down and standing.
- **Physical and Neurological examination:** You will have a physical examination, including a neurological examination.
- **Electrocardiogram (ECG):** A 12-lead electrocardiogram will be performed. This is a painless procedure that measures electrical activity of your heart.

- **Blood drawing (venipuncture):** Blood samples will be collected for routine hematology, chemistry including kidney function tests, liver function tests, thyroid function tests, and uric acid prior to taking the first dose of study drug. Plasma will also be collected for pharmacokinetics (PK), which is how the body uses and gets rid of the drug, pharmacodynamics (PD), which studies how the drug affects the body, and chemicals or proteins that may be associated with the presence of neurodegenerative disease, such as tau and neurofilament proteins (These proteins are found inside nerve cells, called neurons, in the brain).
- **Urine sample:** You will be asked to give a urine sample for a routine urine test.
- **Urine Pregnancy testing (female subjects):** If you are a woman of child-bearing potential, a urine pregnancy test will be done prior to taking the first dose of study drug. Urine pregnancy testing will be repeated at Weeks 8, 12, 20, and 24/ET.
- **Well-being questions:** The study doctor and study staff will ask you and your study partner questions about your memory, your mood, and your everyday life. You will also be asked how you are feeling emotionally, and how you are functioning in your daily life.
- **Memory and cognitive testing:** Memory and thinking tests will be performed and may take up to 110 minutes for you to complete. Some of the testing will be completed on a mobile telephone application. The study team will provide instructions on using the health application.

If you continue to meet all eligibility requirements at baseline, you will be randomized and enrolled in the study. Randomization means that you will be assigned the active study drug (Verdiperstat) or placebo by chance, similar to flipping a coin. A computer program will place you into study drug treatment groups (active drug/placebo). Neither you nor your doctor can choose the group you will be in or will know whether you receive study drug or placebo. If a problem occurs and your study doctor needs to know whether you are receiving study or placebo, he/she will be able to find out this information.

- **Randomization:** You will be "randomized" 3:1 to one of two study groups: Verdiperstat or Placebo. This means that during this study 75% of subjects will receive the active drug and 25% will receive placebo.
  - Verdiperstat Group: Fifteen (15) subjects will be randomized to the active drug.
  - Placebo Group: Five (5) subjects will be randomized to the placebo group.

Study Drug Groups	Chance of Receiving Each Type of Study Drug
Verdiperstat	15 out of 20 subjects (approximately 75% chance)
Placebo (inactive substance)	5 of 20 subjects (approximately 25% chance)

- **Study Drug Administration (First dose):** You will take your first dose of study drug (Verdiperstat or placebo) in the clinic on Day 1. You must swallow the pills whole without crushing or chewing them. During the first week of study drug dosing, you will take one (1) dose per day to see how you are tolerating the study drug. Then, the second week of study dosing you will start taking two (2) doses of study drug each day. The study staff will provide instructions on how to take the study drug at home. Your study doctor and staff will review and discuss a list of prohibited medications that may not be taken while you are participating in the study.
- **Post-First Dose Observation**: After taking your first dose you will need to remain in the clinic for approximately 3 hours to make sure you are feeling well and that you do not have a reaction to the study drug. During the observation you will be regularly asked how you are feeling. Your vital signs and an ECG will be recorded at the end of the 3-hour observation period.
- **Study Drug Dispensing:** You will receive enough study drug tablets to last until your next study visit. You and your study partner will be asked to bring all used and unused study drug bottles to each follow-up visit. The research staff will give you instructions on how to take the study drug and how to store the study drug at home.
- **Study Diary**: You will be given a study diary and asked to record your daily use of study drug and any symptoms you experience, as well as any other medications you take. You will be asked to bring the diary to each visit so the study staff can review it with you and your study partner.

End of Week 2 Visit: You will return to the clinic at the end of 2 weeks for the following:

- **Symptom and medication review:** You will be asked how you are feeling and whether you have had any problems since the last visit. You will be asked about any changes in your medications, vitamins or other supplements.
- **Study Diary Review:** You and your study partner will be asked to bring all used and unused study drug bottles to each follow-up visit. You will also be asked to bring the study diary so the study staff can review it with you and your study partner.

The End of Week 2 Visit may be replaced with video telemedicine assessment at the study doctor's discretion.

End of Weeks 4, 8, 12, 16, and 20 Visits: In this study you will return to the clinic approximately every 4 weeks for the following:

- **Symptom and medication review:** At every visit you will be asked how you are feeling and whether you have had any problems since the last visit. You will be asked about any changes in your medications, vitamins or other supplements.

- **Measurement of your vital signs:** Your blood pressure, pulse, respiratory rate, and temperature will be measured after resting for 5 minutes. Your blood pressure and heart rate will be taken while you are lying down and standing.
- Your weight will also be recorded.
- **Urine Pregnancy testing (female subjects):** If you are a woman of child-bearing potential, a urine pregnancy test will be done at Weeks 8, 12, and 20.
- **Urine sample:** You will be asked to give a urine sample for a routine urine test.

- **Study Drug Dosing:** At the End of Week 12 Visit, you may be asked to fast and you will be asked to hold your morning dose of study drug so that this dose can be supervised in the clinic and aligned with a planned blood draw. The study staff will instruct you on fasting and the timing of morning study drug dose and blood sample collection. At End of Weeks 4, 8, 16, and 20 Visits you will take the morning dose of study drug at home before you come to the research center for your visit.
- **Blood drawing (venipuncture):** Blood samples will be collected for routine hematology, chemistry including kidney function, liver function, thyroid function, and uric acid tests. Additionally, at Week 12 two blood samples for plasma PK will be collected (just prior to and approximately 3 hours after your morning dose is taken) and one blood sample for plasma PD will be collected (approximately 3 hours after your morning dose is taken). At Week 20 a coagulation blood test will be performed.
  - **Well-being questions:** The study doctor will ask you and your study partner many questions about your memory, your mood, and your everyday life. You will also be asked how you are feeling emotionally, and how you are functioning in your daily life.
- **Physical and Neurological examination:** You will have a physical and neurological examination by the study doctor.
- **Electrocardiogram (ECG):** A 12-lead electrocardiogram will be performed.
- **Study Diary Review:** You will be asked to bring the study diary so the study staff can review your study drug dosing and symptoms with you and your study partner.
- **Study Drug Dispensing:** At each visit you will receive enough study drug to last until your next study visit. You and your study partner will be asked to bring all used and unused study drug bottles to each follow-up visit.

Week 24 – End of Study Drug Treatment /or Early Discontinuation Visit:

You will return to the clinic at the end of the 24-week study drug dosing period for the procedures listed below. The End of Treatment procedures may take place over several days if necessary. You may be asked to fast and you will be asked to hold your final morning dose of study drug so that this dose can be supervised in the clinic and aligned with a planned blood draw. The study staff will instruct you on fasting and the timing of the morning study drug dose and blood sample collection.

- **Symptom and medication review:** You will be asked how you are feeling and whether you have had any problems since the last visit. You will be asked about any changes in your medications, vitamins or other supplements.
  - **Study diary review:** You will be asked to bring the study diary so the study staff can review with you and your study partner. The study staff will collect the used and unused study drug bottles at this time.
  - **Measurement of your vital signs:** Your blood pressure, pulse, respiratory rate, and temperature will be measured after resting for 5 minutes. Your blood pressure and heart rate will be taken while you are lying down and standing. Your weight will also be recorded.
  - **Urine Pregnancy testing (female subjects):** If you are a woman of child-bearing potential, a urine pregnancy test will be done.
  - **Urine sample:** You will be asked to give a urine sample for a routine urine test.
  - **Well-being questions:** The study doctor will ask you and your study partner many questions about your memory, your mood, and your everyday life. You will also be asked how you are feeling emotionally, and how you are functioning in your daily life.
  - **Memory and cognitive testing:** Memory and thinking tests will be performed and may take up to 110 minutes for you to complete. Some of the cognitive testing will be completed on a mobile telephone application and the study team will provide instructions on how to use the health application.
  - **Physical and Neurological examination:** You will have a physical and neurological examination by the study doctor.
  - **Electrocardiogram (ECG):** A 12-lead electrocardiogram will be performed.
- **MRI scan procedure:** The MRI scan of your brain must be performed before the lumbar puncture (LP) procedure.
- **Lumbar puncture (spinal tap):** The LP must be performed after the final observed morning study dose. You will be required to remain in bed for approximately one hour following the procedure. You or your study partner will be contacted by telephone approximately 24 hours after the lumbar puncture procedure to see how you feel.
- **Blood drawing (venipuncture):** Blood samples will be drawn from your arm just prior to and approximately 3 hours after your final observed morning study dose for plasma PK and a blood sample will be collected approximately 3 hours after your final dose is taken for plasma PD assessments. Safety labs for routine hematology, chemistry including kidney function, liver function, thyroid function, and uric acid will also be collected.

Final Follow-Up Safety Visit (Week 28):

You will be asked to return to the clinic approximately 4 weeks after the final study drug dose. The following procedures will be performed:

- **Symptom and medication review:** You will be asked how you are feeling and whether you have had any problems since the last visit. You will be asked about any changes in your medications, vitamins or other supplements.
- **Measurement of your vital signs:** Your blood pressure, pulse, respiratory rate, and temperature will be measured after resting for 5 minutes. Your blood pressure and heart rate will be taken while you are lying down and standing. Your weight will also be recorded.
- **Study diary review:** You will be asked to bring the study diary so the study staff can review it with you and your study partner.
- **Physical and Neurological examination:** You will have a physical and neurological examination by the study doctor.
- **Electrocardiogram (ECG):** A 12-lead electrocardiogram will be performed at the final follow-up safety visit.

- **Well-being questions:** The study doctor and study staff will ask you and your study partner questions about your memory, your mood, and your everyday life. You will also be asked how you are feeling emotionally, and how you are functioning in your daily life.
- **Blood drawing (venipuncture):** Blood samples will be collected for routine hematology, chemistry including kidney function tests, liver function tests, thyroid function tests, and uric acid level.

Early Discontinuation: If you discontinue participation in the study early, the study doctor will ask you to return to the clinic within the 4 weeks after the last study drug dose for a safety evaluation. The Early Discontinuation procedures are the same as those listed for Week 24 End of Treatment.

How long will I be in the study?

The total duration of your participation is approximately 8 months long, including a 6-week screening period, a 24-week study drug treatment period, and a follow-up visit 4 weeks after the end of treatment.

Can I stop being in the study?

Yes. You can decide to stop at any time. It is important to tell the study doctor if you are thinking about stopping so that your doctor can evaluate any risks from the study drug and discuss what alternative follow-up care and testing could be most helpful for you.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped. The study doctor will let you know if it is not possible for you to continue in the study for any reason.

If you decide to stop being in the study, or if your study doctor stops you from taking part in the study, your study doctor will ask you to come back for a final study visit.

What side effects or risks can I expect from being in the study?

There are risks to taking part in a research study. Some of the most likely risks of participation in this study include:

Very Common side effect:

- Headache (may affect more than 1 in 10 people, 19%)

Common side effects: (may affect up to 1 in 10 people, 10%)

• Nausea (8%)	• Vomiting (2%)
• Fatigue (feeling tired) (6%)	• Contact dermatitis (inflammation of the skin) (3%)
• Dizziness (5%)	• Presyncope (feeling like you are about to faint) (3%)
• Nasopharyngitis (common cold. upper respiratory infection) (4%)	• Urinary tract infection (UTI) (2%)
• Insomnia (difficult sleeping) (2%)	• Constipation (2%)
• Diarrhea (2%)	• Dizziness-postural (with change in position) (2%)
• Fall (2%)	• Upper respiratory infection (2%)
• Application site irritation/reaction (2%)	• Lethargy (lack of energy and enthusiasm) (2%)
• Pain in extremity (legs/arms) (2%)	• Syncope (fainting) (2%)
• Pain (abdominal [4%] and back [3%])	

In human clinical studies, verdiperstat has been associated with laboratory changes showing decreased thyroid function, including increases in thyroid stimulating hormone (TSH) levels and decreases in free thyroxine (T4) and free triiodothyronine (T3) compared to study subjects receiving placebo. Most study subjects did not have thyroid function test values outside the normal range, and the abnormalities that occurred were mild and returned to normal once verdiperstat treatment was stopped.

There are **Rare but Serious Risks** of participation, like:

- Long lasting side effects, or side effects that never go away
- Death

We'll tell you about the other risks in the below sections of the consent form.

- **Unknown risks:** There may be other risks or side effects that are unknown at this time.
- **Allergic reactions:** As with any drug, an allergic reaction can occur. Allergic reactions can be mild or more serious, and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing. If you think the subject is having an allergic reaction, let the study doctor/study team know right away. He or she will be monitored closely for allergic reactions.
- **Reproductive risks:** You should not become pregnant or father a baby while on this study because the drugs in this study may affect an unborn baby. Women should not breastfeed a baby while on this study. It is important to understand that you need to use birth control while on this study. Check with your study doctor about what kind of birth control methods to use and how long to use them.

If you are a female and could become pregnant (woman of childbearing potential), your study doctor will confirm that you are not pregnant by performing a blood pregnancy test at the screening visit and a urine pregnancy test at baseline (Day 1 prior to first dose). Further, to participate in this trial, you must agree to abstain from sex or use a highly effective birth control that includes two methods of contraception (one of which must be a barrier method) for the duration of the screening period, the 24-week treatment period, and for 30 days after the last study dose. Because Verdiperstat may reduce the plasma levels (dose) of certain hormonal contraceptives, if you are using an estrogen-containing oral hormonal contraceptive, you will be asked to use alternative and/or additional barrier methods of birth control for the time period noted above.

If you are male and not surgically sterilized, you must agree to abstain from sex with women of childbearing potential or if you have sex with a woman of childbearing potential, she must use a highly effective birth control (as defined above for woman of childbearing potential) for the duration of the 24-week treatment period and for 90 days after the last study dose.

You must tell the study doctor as soon as possible if you or your partner becomes pregnant during this study.

What are the other possible risks of taking part in this study?

- MRI scan procedure: During the MRI scan procedure, you will need to lie quietly in the MRI machine while the scanner circles around your head. Some people may experience anxiety while they are in the scanner. Because the MRI machine acts like a large magnet, it could move iron-containing objects in the MRI room during your examination, which could possibly harm you. Precautions have been taken to prevent such an event from happening; loose metal objects, like pocket knives or key chains, are not allowed in the MRI room. If you have a piece of metal in your body, such as a fragment in your eye, aneurysm clips, ear implants, spinal nerve stimulators, or a pacemaker, you will not be allowed into the MRI room and cannot have an MRI. Having an MRI may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia and by the loud banging noise during the study. Temporary hearing loss has been reported from this loud noise. You will be asked to wear ear plugs.

- Radiation risk from optional CT-guided LP: This research study involves exposure to radiation. Not all this radiation exposure is necessary for your medical care and is for research purposes only. Typically, persons in the U.S. receive an annual background dose of radiation of about 3 mSv (a mSv, or millisievert, is a measurement of radiation) from the environment. The additional amount of radiation that you will receive in any 12-month period as a result of participating in this study will be a maximum of 4 mSv, or approximately 1.5 times the yearly natural background. It is unclear whether this amount of radiation may result in a very small increased risk of future cancer. If you have had a lot of x-rays or other procedures involving radiation, you should discuss this with the principal investigator for this study or your regular doctor and consider whether as a result of total radiation exposure, participation in this study is appropriate for you. If you are pregnant or breast feeding, you SHOULD NOT participate in this study. If you have any questions regarding the use of radiation or the risks involved, please consult the physician conducting the study.
- Well-being questions: The study doctor and study staff will ask you and your study partner many questions about your memory, your mood, and your everyday life. The questions may cause anxiety or fatigue.
- Memory and cognitive testing: The tests used to assess your memory and mental performance may sometimes cause anxiety or fatigue.
- Blood drawing (venipuncture): You may have pain, swelling, or bruising around the vein where your blood sample is collected. You may feel dizzy or you may faint during or immediately after your blood is collected. There may be risk of infection. You may get an infection at the place on your body from which the blood is drawn.
- Lumbar puncture (spinal tap): You may experience some pain, discomfort, or bruising as a result of the extraction of cerebrospinal fluid by lumbar puncture. During the lumbar puncture, you will either sit or lie with your knees drawn up to your stomach. You may find this position uncomfortable. You may experience pain or tingling when the anesthetic is injected. There is a possibility of an allergic reaction to the anesthetic. You will feel pressure when the needle is inserted. Some patients may experience headache, nausea, discomfort, and/or pain during the procedure. Rarely, patients may experience vomiting, bleeding into the spinal canal, infection, spinal canal nerve damage, brain damage, or death after the procedure. If you feel unwell or have any unusual discomfort (for example: headache) during or after the lumbar puncture, it is important that you tell the study doctor as soon as possible. Sometimes, after a lumbar puncture, spinal fluid can leak, decreasing the pressure of the spinal fluid. This low pressure causes a headache. A headache after a lumbar puncture can cause severe pain with standing or sitting, and no pain with lying flat. If you have a low-pressure headache, your doctor may first instruct you to rest, lie flat, and drink plenty of fluids. If this does not help, the study doctor may refer you for a ‘blood patch’. During the blood patch procedure some of your own blood is injected in the spinal canal close to the area where the lumbar puncture was performed. This seals the leak of spinal fluid and relieves the headache.

To reduce any potential side effects from the lumbar puncture, we will ask you not to do any strenuous activity for 24 hours after the spinal tap. This includes lifting, bending, doing housework, gardening, or doing exercise such as jogging or bike riding.

Randomization risks: You will be assigned to the study drug or placebo group by chance, and one study group (study drug or placebo) may prove to be less effective or to have more side effects than the other study group. If you are assigned to receive placebo, there will be no chance of direct benefit from taking part in the study.

For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the study?

You may benefit from participating in the study, but this cannot be guaranteed.

What other choices do I have if I do not take part in this study?

You do not have to participate in this study. Your other choices may include:

- Getting treatment or care for your condition without being in a study.
- Taking part in another study.
- Getting no treatment or receiving comfort care to relieve your symptoms and discomfort.

Please talk to your doctor about your choices before agreeing to participate in this study.

Will my medical information be kept private?

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.

There are some important things that you need to know. The Certificate DOES NOT stop reporting that federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate CANNOT BE USED to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate DOES NOT stop disclosures required by the federal Food and Drug Administration (FDA). The Certificate also DOES NOT prevent your information from being used for other research if allowed by federal regulations.

Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

The study staff will do their best to make sure that the personal information in your medical record is kept private. However, total privacy cannot be guaranteed. Your personal information may be given out if required by law. For instance, if study investigators see any evidence of elder abuse

from their contact with subjects, they are required by law to report this information to authorities. In addition, if you share information with the study staff, such as suicidal thoughts, that would make the study doctor concerned about your safety, this information may be shared with your doctor or with other doctors. This information will only be shared so that a plan can be put together to make sure that you are safe and that you receive any needed treatment.

If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Participation in research may involve a loss of privacy, but information about you will be handled as confidentially as possible. **A medical record will be created because of your participation in this study.** Your consent form and some of your research test results will be included in this record. Therefore, your other doctors may become aware of your participation. Hospital regulations require that all health care providers treat information in medical records confidentially.

As part of your participation in clinical research, you may receive related mailings such as educational mailings and scheduling confirmations.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The University of California
- Applicable regulatory authorities involved in keeping research safe for people, such as the U.S. Food and Drug Administration (FDA)

How will my specimens and information be used?

Researchers will use your specimens and information to conduct this study. Specimens and information gathered during this research study will only be used for this study. They will not be shared with other researchers.

Researchers will use your specimens and information to conduct this study. During the study, we may share your specimens and information with other researchers so they can use them for other studies in the future. We will not share your name or any other personal information that would let the researchers know who you are. We will not ask you for additional permission to share this de-identified information.

This research will be partnering with the ALLFTD (www.allftd.org), a non-profit, National Institute of Health-funded collaboration of dementia researchers dedicated to finding a cure for diseases like svPPA. During screening, you will be assigned a National Institute on Aging Global Unique Identifier (GUID) that will be shared with ALLFTD. The purpose of this GUID is to allow for the sharing of deidentified data between the sponsor and ALLFTD. The GUID may also be used for other data-sharing purposes, allowing matching across datasets without providing identifying information.

What are the costs of taking part in this study?

You will not be charged for any of the study activities or the study drug.

Will I be paid for taking part in this study?

You will be provided parking stickers to cover your parking expense at the UCSF public garage when you visit UCSF for study visits. You will also receive a stipend to help cover any expenses you incur in the course of participating in this study, such as gasoline, bridge tolls and meals. The stipend will be $100 per visit for each scheduled visit over the course of the study, including the screening visit. You will be paid $75 for additional MRI and/or lumbar puncture visits. The total amount of stipend payment during the study is approximately $1,000. When you receive your payment from UCSF, you will need to fill out a form acknowledging receipt of the money, and you will need to provide your social security number on this form. Subject payments for research participation are considered taxable income. If you are paid more than $600 total in a calendar year for participation in this study, UCSF will report this income to the IRS.

The study will provide some reimbursement for reasonable travel expenses to come to UCSF for visits. Please talk with the study doctor and staff about what travel expenses may be covered.

What happens if I am injured because I took part in this study?

If you have questions about the factors involved please ask the study physician for more information. It is important that you tell the study nurse or the study doctor if you feel that you have been injured because of taking part in this study. You can tell them in person or call Mary Koestler at (415) 476-0661 or Dr. Peter A. Ljubenkov (415) 502 -7562.

Treatment and Compensation for Injury: If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California, depending on a number of factors. The University does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at (415) 476-1814.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may withdraw from the study at any time by telling the study staff. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your ability to receive medical care. You can still receive medical care from medical facilities associated with your research center. The study doctor may stop you from taking part in the study at any time if he/she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

You have the right to know about any new information that is discovered during the study. The study staff will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact Mary Koestler, RN, study nurse at (415) 476-0661 or your study doctor, Dr. Peter A. Ljubenkov (415) 502 7562.

For questions about your rights while taking part in this study, call the office of the **Committee on Human Research**, UCSF's Institutional Review Board (a group of people who review the research to protect your rights) at **415-476-1814**.

ClinicalTrials.gov is a website that provides information about clinical trials. 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.

CONSENT

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep. You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

Signature of Study Participant Date

Printed name of Study Participant

AND/OR The person being considered for this study is unable to consent for him or herself because he or she is cognitively impaired or is not capable of reading or signing the consent form. I have been asked to give my permission to include this person in this study. I know of no reason why he or she would refuse were it possible to do so. I agree to sign a self- certification of surrogate decision maker form (by signing the surrogate form I am stating I am the best person to make

decisions regarding research participation for the person and will state my relationship to the person and provide my contact information).

Signature of Participant's Legally Authorized Representative Relationship Date

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Printed name of Participant's Legally Authorized Representative

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Signature of Person Obtaining Consent Date

_____

Printed name of Person Obtaining Consent

Schedule of Assessments and Procedures:

Assessment and Procedures	Screen Day -42 to Day 1	Baseline Day 1	End Week 2	End Week 4	End Week 8	End Week 12	End Week 16	End Week 20	End Treatment Week 24 / ET	Final Follow-up Week 28
Informed Consent Form	✓									
Medical history and/or symptom & medication review	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Vital Signs	✓	✓		✓	✓	✓	✓	✓	✓	✓
Physical and neurological examination	✓	✓		✓	✓	✓	✓	✓	✓	✓
ECG	✓	✓		✓	✓	✓	✓	✓	✓	✓
Weight (Height screen only)	✓	✓		✓	✓	✓	✓	✓	✓	✓

Blood drawing and/or urine sample	✓	✓		✓	✓	✓	✓	✓	✓	✓
Well-being questions	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Memory and cognitive testing	✓	✓							✓	
Study drug Dispensing		✓		✓	✓	✓	✓	✓		
Study diary review		✓	✓	✓	✓	✓	✓	✓	✓	✓
Pregnancy testing for Women Child-bearing	✓ blood test	✓ urine test			✓ urine test	✓ urine test		✓ urine test	✓ urine test	
MRI scan	✓								✓	
Lumbar puncture	✓								✓	
Plasma collection for PK/PD		✓				✓			✓	