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

CC#15558: Phase II Trial of Definitive Radiotherapy with Leuprolide and Enzalutamide in High Risk Prostate Cancer

This is a clinical trial, a type of research study. Your study doctor, Hao Nguyen, MD, PhD, or one of his associates at the University of California, San Francisco (UCSF) Department of Radiation Oncology will explain the clinical trial to you.

Clinical trials include only people who choose to take part. Please take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctor.

You are being asked to take part in this study because you have high risk prostate cancer or with pelvic node involvement.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to test the safety of the combination of enzalutamide and leuprolide in patients undergoing standard of care radiation therapy treatment and to determine the response rate of the combination.

Leuprolide is used to treat advanced prostate cancer in men. It is not a cure. Most types of prostate cancer need the testosterone to grow and spread. Leuprolide works by reducing the amount of testosterone that the body makes, but does not completely block the production of testosterone.

Enzalutamide is a drug that can block the binding of testosterone to the receptors on prostate cancer cells. Enzalutamide is approximately 9-fold more effective in blocking testosterone from its receptor when compared to bicalutamide, a drug that is often used in combination with leuprolide. Enzalutamide is approved the US Food and Drug Administration (FDA) for the treatment of metastatic (cancer that has spread) castration-resistant prostate cancer (CRPC). More profound testosterone blockade with the combination of enzalutamide and leuprolide may improve the outcome of patients with high risk prostate cancer. However, the combination of enzalutamide with leuprolide with radiation therapy (radiotherapy) is considered investigational and has not been approved by the FDA.

Astellas Pharma, the makers of enzalutamide, is providing the drug at no cost for the study. The National Comprehensive Cancer Network (NCCN) is providing funding to UCSF to conduct this research trial. UCSF is sponsoring this study.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 53 people will take part in this study at clinical sites in the United States with about 40 people at UCSF.

WHAT WILL HAPPEN IF I TAKE PART IN THIS RESEARCH STUDY?

Patients will receive enzalutamide in combination with leuprolide for about 24 months along with conventional whole pelvis radiation therapy for 25 treatments (5 weeks). Following the initial radiation therapy treatments, patients will undergo a radiation boost to the prostate with internal radiation (termed as brachytherapy). This form of radiation therapy is part of the standard of care.

After radiation therapy is completed, you will be seen by your radiation oncologist at least every three to six months for the first 24 months. This is also the standard of care follow-up for patients with prostate cancer. At each visit, you will be asked questions about your general health, changes in health, and symptoms related to treatment and to your prostate cancer. You will also be asked to complete quality of life questionnaires regarding your overall general well-being, urinary symptoms, bowel symptoms, and sexual function.

Before you begin the main part of the study...

You will need to have the following exams, tests or procedures to find out if you can be in the main part of the study. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

You must complete your screening procedures within 14 weeks prior to receiving the treatment, unless otherwise indicated. Your screening visit may take up to 4-5 hours depending on which procedures you have. The following procedures will occur:

- Physical exam, including review of your full medical history
- Standard of care staging exams which may include MRI, Sodium Flouride Pet/CT, or bone scan.
    - For the MRI, you may be given a "contrast material" (a special dye that makes it easier for doctors to see different tissues in your body). Gadolinium is contrast material that causes some tumors to appear much brighter than normal tissue on MRI scans (these tumors may not be visible without gadolinium). The contrast material may be given to you in your arm through an intravenous catheter (a tiny tube inserted into a vein). You will then lie down on a narrow bed which will be placed in a tunnel that is 6 feet long by 22 inches wide and open at each end. You will lie there quietly for about one hour, during which time you will hear a loud machine-

like noise. The MRI scan is done in the radiology department and takes approximately an hour and a half to complete.

- For the Sodium Flouride (NaF) Pet/CT, this is a special type of scan of the entire skeletal system that produces images of the bones. These images are used to detect areas of abnormal bone growth associated with tumors that may have spread from different organs, such as the prostate. You will be asked to not eat for six hours prior to the scan and to drink at least two large glasses of water within one hour of the study. Your NaF PET/CT scan will begin with an injection of a radioactive substance into a vein in your arm. You will be asked to rest quietly for a period of time (usually about 60 minutes) as the radioactive substance circulates throughout your body. After this time, you will be positioned within a large ring (similar to a big donut hole) on a scanning bed. Once positioned properly, the bed will move you into the scanner. As pictures are being taken, you will be asked to remain very still so clear images will be taken. The imaging time takes about 30 minutes.
- A bone scan is a test that makes detailed images of your bones and any tumors on them. Before the bone scan a small amount of radioactive substance is injected into your vein. About 3 hours later you will lie on a table under a machine which will make an image of your bones. The test itself will take about 1 hour, but the whole process takes up to 4 hours.

- Blood (about 2-3 tablespoons) will be drawn
  - For routine safety tests
  - To check for hepatitis B and C
  - To check liver function
  - To check PSA levels - this test is used to measure the amount of protein produced by the prostate that is in your blood and can help determine if you are responding to treatment
  - To check testosterone levels
- Prostate Biopsy – You will be given an enema at least 1 hour prior to the procedure, and you will be given oral antibiotics at least 30 minutes prior to the procedure. You will then undergo a Transrectal Ultrasound (TRUS). A transrectal ultrasound is routinely performed at the time of initial diagnosis of prostate cancer, at the time of gold marker placement to improve the accuracy of patient setup before radiation treatment delivery, and at the time of brachytherapy. Thus, an ultrasound will be performed as part of routine care for patients with high-risk prostate cancer undergoing radiation therapy. The test is safe and simple to perform. As you lie on your right or left side on an examination table, an image of the prostate will be obtained. A small probe, the size and shape of an index finger and covered with a rubber shield, is gently inserted into your rectum. You will feel a sensation similar to a rectal examination.

  The doctor will then perform a prostate biopsy which can be obtained accurately with the guidance of ultrasound. The biopsy is performed through the rectum

with a needle. No numbing medication is necessary for this procedure since the needle is thin and the rectal wall is not sensitive to pain. You may feel some pressure, however, or experience a mild stinging sensation in your prostate when the doctor performs the biopsy. You can leave immediately after the procedure.
    - If you have had a prostate biopsy and ultrasound within the past 6 months, you may not need to repeat the procedures.

For research purposes

- Questions about how your disease is affecting your daily life
- EPIC 26, PROMIS, and EQ-5D Questionnaires - You will be asked to complete questionnaires to find out how prostate cancer affects your quality of life.
- Blood (about 3-4 tablespoons) will be drawn for research purposes. Blood will be used to identify potential changes in the genes (DNA) associated with enzalutamide resistance, gene expression patterns, and any changes in the immune response with enzalutamide treatment
- Collection of leftover, "archival", tissue from a previous prostate biopsy if available. Tissues collected from a prior biopsy and during your participation in this study will be used for genetic testing to evaluate whether changes in a person's DNA are involved in the response to enzalutamide. The tissue will also be used to evaluate gene (DNA) expression and changes and their relationship to the immune response. Please see the About Using Tissue For Research at the end of this consent form for more information.

During the main part of the study...
If the exams, tests and procedures show that you can be in the main part of the study, and you choose to take part, then you will have the procedures listed below.

Day 0 – begin androgen deprivation therapy with enzalutamide and leuprolide treatment

- Enzalutamide – Once every three months, you will receive a 3 month supply of enzalutamide during your clinic visits. Enzalutamide can be taken with or without food once a day. Please take the medication at the same time each day. Swallow capsules whole. Do not chew, dissolve, or open the capsules.

- Leuprolide - You will receive an injection of leuprolide during your clinic visits. The administration schedule for leuprolide may vary per patient; it can be given monthly or every 3-, 4-, or 6-months. Your study doctor will let you know which schedule you will follow.

4-6 weeks after initiation of androgen deprivation therapy

This visit will take about 2-3 hours. The following assessments will be performed.

- Blood (about 2-3 tablespoons) will be drawn
    - For routine safety tests
    - To check liver function
    - To check PSA levels

    - To check testosterone levels
- Radiation Treatment Planning
    - Your radiation doctor (radiation oncologist) will schedule a special CT scan (CT simulation scan). This scan will be done in a simulated treatment position so that your treating team can appropriately design the radiation treatment. Procedure will take approximately 1 hour.

      A CT scan uses special x-ray equipment to make detailed pictures of body tissues and organs. For these scans, no intravenous (IV) contrast will be necessary. You will lie flat on a table that will move you into the CT scan machine. You will be asked to lie still and may be asked to hold your breath for a few seconds. The CT scan is done in the radiology department and takes about half an hour.
    - At the time of CT simulation, patients will be immobilized with a custom mold. While immobilized, the patient will be scanned. CT scan images obtained in this treatment position are sent to a radiation therapy-planning computer where your oncologist and his team design and calculate the appropriate radiation treatment. These calculations are double-checked and verified before the treatment starts. This process may take several days to complete.
    - On your first treatment day, radiation therapists will place you in exactly the same position as you were on the simulation CT scan.
- Prostate biopsy – may be performed per standard of care if the study doctor suspects your cancer has recurred

<u>For research purposes</u>

- Review of any side effects
- Blood (about 3-4 tablespoons) will be drawn for research purposes.

8 weeks after initiation of androgen deprivation therapy

This visit will take about 1 hour. The following assessments will be performed.

- Begin radiation therapy – 5 days a week for up to 5 weeks
    - You will be monitored for any side effects weekly by the radiation oncologist

<u>For research purposes</u>

- Review of any side effects
- Questionnaires – about 5 days before the start of radiation therapy

Phase 2 Radiation Therapy

This visit will take about 2-3 hours. The following assessments will be performed.

- You will undergo a radiation boost to the prostate with internal radiation (termed as brachytherapy).
- Blood (about 2-3 tablespoons) will be drawn
    - For routine safety tests
    - To check liver function
    - To check PSA levels
    - To check testosterone levels
- Prostate biopsy – may be performed per standard of care if the study doctor suspects your cancer has recurred

For research purposes

- Review of any side effects
- Blood (about 3-4 tablespoons) will be drawn for research tests

When you are finished receiving radiation…
You will be asked to come into the clinic for follow up on your health status. The first visit will be 6 weeks after the end of your radiation treatment and then month 3-4, month 6, month 12, month 18, month 24, and month 36. If you no longer wish to participate in this follow-up period, please let your study doctor know. The following tests and procedures will be done during the clinic visits; the visits will take less than 1 hour.

- Physical exam, including review of your medical history
- Blood (about 2-3 tablespoons) will be drawn
    - For routine safety tests
    - To check liver function
    - To check PSA levels
    - To check testosterone levels
- Standard of care staging exams which may include MRI, NaF Pet/CT, or bone scan- to be performed if blood tests indicate PSA levels are rising

For research purposes

- Review of any side effects
- Questionnaires
- Blood (about 3-4 tablespoons) will be drawn for research tests – only at month 3-4

Study location: All study procedures will be done at the Helen Diller Family

Comprehensive Cancer Center.

HOW LONG WILL I BE IN THE STUDY?

You will receive enzalutamide and leuprolide for up to 2 years as long as you do not have severe side effects or until you decide to withdraw your consent to participate in this study or the study is closed. Though clinical guidances indicate that patients with high risk prostate cancer have the option of receiving androgen deprivation therapy anywhere from 2-3 years; at UCSF, the standard duration for hormone therapy is 2 years. The 2 year course of therapy is used in many institutions nationally and was also the standard dose used on the most recent national cooperative group clinical trial. There is no data that a period of greater than 2 years is beneficial over 2 years. The side effects of androgen deprivation therapy may also affect the your quality of life. You will receive radiation treatment for approximately 5 weeks. After you are finished with radiotherapy ask you to visit the office for follow-up exams for up to 3 years.

CAN I STOP BEING IN THE STUDY?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop they will tell you how to stop safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from the study treatment can be checked by your doctor. Another reason to tell your doctor that you are thinking about stopping is to talk about what follow-up care and testing could be most helpful for your cancer treatment.

The study doctor may stop you from taking part in this study at any time if they believe it is in your best interest, if you do not follow the study rules, or if the study is stopped.

WHAT SIDE EFFECTS OR RISKS CAN I EXPECT FROM BEING IN THE STUDY?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop radiation. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death.

You should talk to your study doctor about any side effects that you experience while taking part in the study.

Risks and side effects related to the standard radiation therapy regimen

Likely
- Feeling tired
- Increased urinary frequency
- Burning upon urination
- Urinary hesitancy
- Urinary urgency
- Loose stools or diarrhea

Less Likely
- Nausea
- Vomiting
- Decreased production of blood cells that may cause you to get infections

Rare, but Serious
- Blockage or swelling of the intestines
- Fractures in bones of the spine
- Pain caused by nerve swelling
- Ulceration of the rectum or bladder
- Skin toxicity

Risks and side effects related to leuprolide

Likely
- vasomotor hot flashes
- edema
- gynecomastia
- bone aches
- gastrointestinal disturbances
- decreased libido
- erectile dysfunction

Less likely
- weight gain
- depression
- dizziness
- loss of bone density
- anemia
- increased thirst and urination
- unusual taste in the mouth
- skin redness or hives

- pain at injection site
- and muscle mass and strength loss
- hair changes
- penile length and testicular volume loss
- increased cholesterol
- hypertension
- diabetes exacerbation
- emotional lability
- nausea
- vomiting
- rarely - allergic generalized rash and difficulty breathing, osteopenia or osteoporosis (bone mineral loss)

Rare but serious

- heart attack
- stroke
- bone fracture from osteoporosis (bone mineral loss)

Risks and side effects related to enzalutamide

Likely

- Fatigue (tiredness)
- Back pain
- Diarrhea
- Joint pain
- Hot flashes
- Peripheral edema (swelling of the legs, ankles, arms, etc)
- Muscle and bone pain
- Headache
- Upper/lower respiratory infection (cough)
- Muscle weakness
- Dizziness
- Insomnia (being able to sleep at night)
- Spinal cord compression and cauda equina syndrome (symptoms of cauda equine include but are not limited to severe back pain, loss of sensation around your pelvis and midsection, unable to hold your urine or bowels, and sexual dysfunction)
- Hematuria (blood in your urine)
- Paresthesia (tingling or prickling sensation on your skin)
- Anxiety
- Hypertension (high blood pressure)

Less likely

- Falls, and fractures caused by falling
- Dry skin
- Itchiness
- Thinking or memory problems
- Hallucinations (seeing or feeling things that are not there)
- Heightened reactions by the body's immune system, which can sometimes lead to fluid build-up in the face, tongue, upper-throat, or lip
- Narrowing of the blood vessels that lead to your heart, which can result in not enough blood supply to the heart, and sometimes can be fatal (ischemic heart disease)

Rare but serious

- Brain disorder characterized by headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome)
- Seizures (convulsions)
- Hemolytic Anemia (a condition in which red blood cells are destroyed and removed from the bloodstream before their normal lifespan is over).

Due to this potential risk of seizure, please inform your study doctor if you have ever had a condition that may increase the risk of seizures, such as brain injury or tumor; or history of alcoholism. The risks related to the drug that are listed above are the same regardless of whether you receive enzalutamide by participating in the study or not.

There are some medicines that are known to increase the chance of having a seizure. These medicines include but are not limited to:

- Aminophylline/theophylline
- Atypical antipsychotics (e.g., clozapine, olanzapine, risperidone, ziprasidone)
- Bupropion
- Lithium
- Pethidine
- Phenothiazine antipsychotics (e.g., chlorpromazine, mesoridazine, prochlorperazine, thioridazine)
- Tricyclic and tetracyclic antidepressants (e.g., amitriptyline, desipramine, doxepin, imipramine, maprotiline, mirtazapine)

Study Drug Combination risks: The side effects of the combination of enzalutamide, leuprolide, and radiation therapy are not yet known. It is possible that this combination of drugs will cause new or more serious side effects than taking these drugs separately. You will be monitored closely for side effects and your doctor may change your medications if it appears that this combination is causing serious side effects. You should tell your doctor about any side effects you experience while on this study. When

additional information about side effects is known, you will be notified of any further study drug related effects.

Blood Drawing (venipuncture) risks: Drawing blood may cause temporary discomfort from the needle stick, bruising, and infection.

Questionnaire risks: Answering the Quality of Life questionnaire may be an inconvenience. Some of the questions may remind you of unpleasant aspects of your therapy or disease, and you may experience some discomfort, anxiety or distress in answering such questions. You are free to decline to answer any questions you do not wish to answer, or to stop participating at any time.

Prostate biopsy risks: If you are taking blood thinners, such as aspirin, persantine, or coumadin, you should notify your doctor prior to the TRUS/biopsy. These medicines may cause serious bleeding complications after the biopsy, and will need to be stopped at least one week before the biopsy. Even without being on these medications there is a small (less than 5%) but real risk of bleeding from the biopsy site. Other risks include pain associated with the procedure, and infection despite the administration of antibiotics.

You will need to avoid heavy exercise or pressure on the prostate (bicycle riding, etc.) or sexual activity for 24 hours. You may notice some blood in your urine, stools, or semen for several days. You will need to take all of the antibiotics even if you have no symptoms. If you develop a fever higher than 101 degrees with chills, or you continue to have a large amount of blood in your urine or stool, you should notify your doctor immediately or go to the hospital emergency room.

Genetic testing of tissue samples risks: Genetic information about your tumor that results from this study does not have medical or treatment importance at this time, so you will not receive the results of this testing. However, there is a risk that information about taking part in a genetic study may influence insurance companies and/or employers regarding your health. Since some genetic variations can help to predict the future health problems of you and your relatives, this information might be of interest to employers, health providers, insurance companies, and others. Patterns of genetic variation also can be used by law enforcement agencies to identify a person or his/her relatives. Therefore, your genetic information potentially could be used in ways that could cause you or your family distress, such as by revealing that you (or a relative) carry a genetic disease or by leading to the denial of employment or insurance for you (or a relative). To further safeguard your privacy, genetic information obtained in this study will not be placed in your medical record.

Radiation/Scan Procedures:

- **Radiation risks:** This study involves exposure to radiation. This radiation exposure is part of routine clinical care and is not related to research. You will not receive additional radiation as a result of participating in this study. The goal of the study is to determine whether the radiations risks occur less frequently with the shorter treatment compared to standard treatment. If you have any questions regarding the use of radiation or the risks involved, please consult the physician conducting the study.

- **MRI risks:** Because the MRI machine acts like a large magnet, it could move iron-containing objects in the MRI room during your examination, which in the process 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. This is why you will be asked to wear earplugs. At times during the test, you may be asked to not swallow for a while, which can be uncomfortable.

  Contrast agent (gadolinium) risks: A few side effects of gadolinium injection such as mild headache, nausea, and local pain may occur. Rarely (less than 1% of the time) low blood pressure and lightheadedness occurs. This can be treated immediately with intravenous fluids. Very rarely (less than one in one thousand), patients are allergic to gadolinium. These effects are most commonly hives and itchy eyes, but more severe reactions have been seen which result in shortness of breath.

  Patients with severe kidney disease sometimes have a bad reaction to gadolinium contrast. The condition is called nephrogenic systemic fibrosis (NSF). It can cause skin to tighten or scar and can damage internal organs. Sometimes it can be life-threatening. There are no reports of NSF in patients with normal kidney function. Before you have a MRI scan requiring an injection of gadolinium contrast, you will have a blood test in order to check the function of your kidneys. Based on your medical history and the results of the test, a doctor will decide whether it is safe for you to undergo the MRI scans.

- **CT scan risks:** CT scans involve the risks of radiation (see above).
  Having a CT scan may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia when placed inside the CT scanner, or by lying in one position for a long time.

- **NaF Pet/CT scan risks:** The PET/CT scan exposes your body to radiation, see radiation risk above. The radiation levels come from a tracer which is a radioactive chemical injected into a vein in your arm. The tracer lets the doctor see how your cells are functioning and the radiation levels are very low. You may have an allergic reaction to the chemical used in the scan. For some patients, having to lie still on the scanning table for the length of the procedure may cause some discomfort or pain. After the scan your arm may be a little bit sore or have

some redness where the IV was placed in your arm. The radioactive solution does not remain in your system for a long period of time. However, you should wait 2 hours before holding an infant or getting close to a pregnant woman to avoid exposing them to radiation. You should drink fluids after the scan to help remove the solution from your system.

Reproductive risks: You should not father a baby while on this study because the drugs in this study can affect an unborn baby. It is important to understand that you need to use birth control while on this study and for up to 4 months (120 days) after the last dose of study drug or agree to completely abstain from intercourse. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study.

Unknown Risks: The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

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

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

Taking part in this study may or may not make your health better. We do know that the information from this study will help doctors learn more about the combination of enzalutamide and leuprolide along with radiotherapy as a treatment for cancer. This information could help future cancer patients.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?

Your other choices may include:

- Getting radiation treatment or care for your cancer without being in a study (fractionated radiation therapy with or without leuprolide)
- Taking part in another study
- Getting comfort care, also called palliative care - this type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer; comfort care does not treat the cancer directly, it works to improve how you feel and keep you as active and comfortable as possible
- Getting no treatment

Your physician will discuss these other options with you. Please talk to your doctor about your choices before deciding if you will take part in this study.

WILL MY MEDICAL INFORMATION BE KEPT PRIVATE?

We will do our best to make sure that the personal information in your medical record is kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

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

- Astellas Pharma and their associates
- National Comprehensive Cancer Network (NCCN)
- The National Cancer Institute (NCI) and other government agencies, e.g., the Food and Drug Administration (FDA), involved in overseeing research
- The University of California

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.

California regulations require laboratories to report new cases of HIV, hepatitis B, and hepatitis C infection to the county public health department. The reports include the patient's name, social security number, and other identifying information. Information about these new infections is used to track these diseases statewide and nationwide. Other than this required reporting, your results will be treated confidentially by the study staff. Personally identifying information will not be reported to other departments or agencies.

WHAT ARE THE COSTS OF TAKING PART IN THE STUDY?

You and/or your health plan/insurance company will need to pay for some or all of the costs of treating your cancer in this study. Some health plans will not pay these costs for taking part in studies. Check with your health plan/insurance company to find out what they will pay for. Your study doctors or their clinical staff will obtain authorization from your insurance company prior to beginning your treatment. Taking part in this study may or may not cost you or your insurance company more than the cost of getting regular cancer treatment.

Astellas Pharma is supplying enzalutamide free of charge. You will not be billed for any of the tests or procedures required specifically by the study. These tests and procedures noted above as "for research purposes" (questionnaires and blood draw for research) in this consent form. Other procedures, which are also done in this research

study but are part of your routine care, will be paid for by you or your insurance. This includes leuprolide, radiation therapy, scans, blood tests, and physical exams that are considered part of the standard treatment for your cancer.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call **1-800-4-CANCER (1-800-422-6237)** and ask them to send you a free copy.

WILL I BE PAID FOR TAKING PART IN THIS STUDY?

You will not be paid for taking part in this study.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?

It is important that you tell your study doctor Hao Nguyen, MD, PhD if you feel that you have been injured because of taking part in this study. You can tell him in person or call him [redacted].

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 leave the study at any time. 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 medical care. You can still get your medical care from our institution.

We 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, concerns, or complaints you have about this study. Contact your study doctor Hao Nguyen, MD, PhD [redacted]

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the Office of the Committee on Human Research at 415-476-1814.

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.

****

Please note: This section of the informed consent form is about additional research studies that are being done with people who are taking part in the main study. You may take part in these additional studies if you want to. You can still be a part of the main study even if you say "no" to taking part in any of these additional studies.

About Using Blood and Tissue For Research

While you are participating in this study, you will have a series of biopsies performed and blood drawn specifically for research purposes. The study team will collect leftover tissue from the biopsy procedures and blood drawn for research for genetic testing to evaluate whether changes in a person's DNA are involved in the response to enzalutamide. The tissue and blood samples will also be used to evaluate gene (DNA) expression and changes and their relationship to the immune response. The tissue and blood samples will be stored indefinitely at UCSF. All samples will be de-identified (your name and any identifiable information will not be included with the samples) and labeled with a case number. The study team would like your permission to conduct future research to learn more about cancer and other diseases on the stored samples.

Reports about research done with your tissue and blood sample will not be given to you or your doctor. These reports will not be put in your health record. The research will not have an effect on your care.

Things to Think About

The choice to let us perform additional future research on the stored samples is up to you. No matter what you decide to do, it will not affect your care.

If you decide now that additional research can be performed, you can change your mind at any time. Just contact the study doctor Hao Nguyen, MD, PhD at the following address, and let him know that you do not want him to use your tissue and blood samples. Then any samples that remain will no longer be used for future research.

Hao Nguyen, MD, PhD
University of California San Francisco
[redacted]

In the future, people who do research may need to know more about your health. While UCSF may give them reports about your health, it will not give them your name, address, phone number, or any other information that will let the researchers know who you are.

Your tissue and blood samples will be used only for research and will not be sold. The research done with your stored samples may help to develop new products in the future. You will not be paid for allowing your blood and tissue samples to be used in research even though the research done with your samples may help to develop new products in the future. You will not receive any payment or financial benefit from any products, tests, or discoveries derived from these samples.

Benefits

The research that may be done with your tissue and blood samples is not designed specifically to help you. It might help people who have cancer and other diseases in the future.

The benefits of research using tissue and blood include learning more about what causes cancer and other diseases, how to prevent them, and how to treat them.

Risks

The greatest risk to you is the release of information from your health records. We will do our best to make sure that your personal information will be kept private. The chance that this information will be given to someone else is very small.

Making Your Choice

Please read each sentence below and think about your choice. After reading each sentence, put your initials in the "Yes" or "No" box. If you have any questions, please talk to your doctor or nurse, or call our research review board at 415-476-1814. No matter what you decide to do, it will not affect your care.

I allow additional research to be performed on my tissue and blood samples in the future.

YES	NO

****

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.

Date	Participant's Signature for Consent
Date	Person Obtaining Consent
Date	Witness Signature (Only required if the participant is a non-English speaker)