PRINCIPAL INVESTIGATOR: James L. Gulley, M.D., PhD.

STUDY TITLE: A Phase I/II Study of Immunotherapy Combination BN-Brachyury Vaccine, M7824, N-803 and Epacadostat (QuEST1)

STUDY SITE: NIH Clinical Center (CC), NCI

Cohort: Affected patients

Consent Version: 05/17/2024

WHO DO YOU CONTACT ABOUT THIS STUDY?

James Gulley, MD, PhD
Phone: [redacted]
Email: [redacted]

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

The remaining document will now describe the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with you about the information in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research interventions in which they would want to participate. Take the time you need to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

If the individual being asked to participate in this research study is not able to give consent to be in this study, you are being asked to give permission for this person as their decision-maker. The term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research, throughout the remainder of this document.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

Immunotherapy drugs are being studied for their potential to boost the body's immune response to cancer. Scientists and doctors think that combining these treatments will make them more effective than when used alone. This may be true for many types of cancer, including castration-resistant prostate cancer (CRPC). In this study, participants will receive treatment combination of either 2, 3, or 4 different immunotherapy drugs (BN-brachyury, M7824, N-803 and Epacadostat).

BN-brachyury, M7824, N-803 and Epacadostat are all investigational (have not been approved by the FDA) immunotherapy drugs.

Generally, these treatments are all thought to help the body's immune system fight cancer in different ways.

M7824 can attach to many different types of cells in the body. When it is attached to cancer, it can make it easier for your immune system to destroy the cancer. When attached to immune cells, it can increase the body's immune response. M7824 has not been used to treat your type of cancer before, therefore we do not know whether or not it will work. M7824 has been tried in other types cancers. Recently, the manufacturer of the drug closed 3 large studies because the drug was shown not to help those patients more than standard therapies. In addition, in some cases it seemed like the drug might make the cancer grow faster. However, the type of cancer treated in those studies was not the same as your cancer.

N-803 can supercharge different types of immune cells that kill tumor cells. It can also increase the numbers of these cancer-fighting cells.

BN-Brachyury is cancer vaccine designed to create immune cells that can recognize and kill certain types of cancer.

Cancer can create chemicals within the body that make it more difficult for the immune system to attack cancer. **Epacadostat** is a drug that blocks production of those chemicals.

In this study, we will investigate the safety of using BN-brachyury, M7824, N-803 and Epacadostat given in different combinations and whether this combined treatment will cause your tumors to shrink.

This study has two parts: a phase I and a phase II. In phase I, we are going to evaluate the safety of using M7824 in combination with N-803. Increasing doses of N-803 will be given to patients in the study to find the highest dose of N-803 that people can tolerate when given in combination with M7824.

In phase II we will first evaluate safety of different combination of drugs: BN-brachyury + M7824, BN-brachyury + M7824 + N-803, BN-brachyury + M7824 + N-803 + Epacadostat. If safe, these combinations will be further evaluated to find a combination which will be the most effective in making your tumors shrink.

WHY ARE YOU BEING ASKED TO TAKE PART IN THIS STUDY?

You are being asked to take part in this research study because your prostate cancer has spread to other parts of your body, and your disease is no longer responding to hormonal therapy or you have a different type of cancer that has metastasized to other parts of your body.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 113 subjects will take part in this study. Approximately 18 participants will be enrolled in the phase I part and approximately 75 participants will be enrolled in the phase II part.

DESCRIPTION OF RESEARCH STUDY

For your safety, some medications and therapies are not allowed during the study. You should tell the study doctor before you take any new medications (includes prescription, herbal, and over-the-counter remedies) or start a new therapy during the study. Please notify the study doctor if you are not willing to have a blood transfusion or receive blood products.

If you agree to take part and have signed the informed consent form, you will undergo screening tests and procedures to see if you qualify for the study. This is known as the Screening Period. These tests and procedures may be done prior to signing this consent. Not everyone who wants to be in the study will be able to join.

Before you begin the study

Before you begin this study, you will need to have the following exams and tests during the screening period to make sure you are eligible for this study. The exams and tests are part of regular cancer care. If you have had some of the tests recently, they may not need to be repeated. If you are not eligible, you will not be able to participate in the study.

- A review of any past or current medical conditions, medicines you are taking and cancer history.
- Physical examination, including height, weight, and vital signs.
- Review of your symptoms and your ability to perform your normal activities.
- Imaging Assessments – either a CT (a series of x-ray images taken of parts of your body) or if you cannot have a CT scan, MRI (magnetic testing, which does not involve any radiation).. These will be used to examine your chest, abdomen and pelvis. If your doctor thinks this is needed, you might have additional imaging of your bones. A bone scan is an imaging test that helps detect cancer that has spread (metastasized) to the bone.
    - Magnetic resonance imaging (MRI) is an alternative to CT scan that is used in some situations. MRI is safe and does not cause any side effects. MRI uses a strong magnetic field and radio waves to take pictures of your body. The MRI scanner is a metal cylinder surrounded by a strong magnetic field. During the MRI, you will lie on a table that can slide in and out of the cylinder. We will place soft padding or a coil around your head. You will be in the scanner about 30 minutes. You may be asked to lie still for up to 30 minutes at a time. While in the scanner you will hear loud knocking noises, and you will be fitted with earplugs or earmuffs to muffle the sound. You will be able to communicate with the MRI staff at all times during your scan, and you may ask to be moved out of the machine at any time.
- You will have about 1 tablespoon of blood drawn for:
    - routine blood tests to find out if you have low blood counts, and if your liver, kidneys, and other organs are working well
    - tests for HIV, Hepatitis B and Hepatitis C

  - PSA and Testosterone level
- Routine urinalysis
- You will be asked to provide confirmation of your diagnosis.
- EKG: a test that is performed while you lie still for about 5 minutes. It involves placing electrodes (small stickers that are attached to wires that go to the machine) on the chest and arms/legs and recording the electrical activity of your heart

- HIV, Hepatitis B, and Hepatitis C Testing

As part of this study, we will test you for infection with the human immunodeficiency virus (HIV), the virus that causes AIDS and Hepatitis B and C. If you are infected with HIV, Hepatitis B or C you will not be able to participate in this study. We will tell you what the results mean, how to find care, how to avoid infecting others, how we report HIV infection, and the importance of informing your partners at possible risk because of your infection.

During the study

Depending on time when you are entering the study, you will have treatment combination of two, three or four drugs: M7824 + N-803, BN-brachyury + M7824, BN-brachyury + M7824 + N-803 or BN-brachyury + M7824 + N-803 + Epacadostat.

You will be treated with combination of drugs until your disease gets worse. The treatment might be interrupted prematurely if you have unacceptable side effects or if in the opinion of the Investigator your disease worsened to the point when these drugs do not help you anymore.

If you cannot tolerate treatment of combination you receive, or if your disease gets worse, you will not get another combination and will be taken off all treatments on this protocol.

For all Participants:

M7824 will be administered to you through an IV (intravenous catheter, a small plastic tube that is put into a vein, usually in your arm) once every 2 weeks (2 weeks = 1 Cycle). This is given to you as an outpatient.

N-803 will be administered to you as a single subcutaneous injection once every 2 weeks (2 weeks = 1 Cycle). You will be given an Injection Site Reaction Diary to complete for each cycle. In the diary, you will be asked to record any skin changes at the injection site. Please bring the diary with you at every study visit.

BN-brachyury will be administered to you as four subcutaneous injections to different limbs. Two priming doses will be administered 2 weeks apart, Day 1 of Cycle 1 and Day 1 of Cycle 2 (2 weeks = 1 Cycle). Two weeks later, the first booster dose will be administered, then every 4 weeks for 6 months, then every 3 months until reaching 2 years. After 2 years you will receive the injections every 6 months.

Only for Participants who will receive Epacadostat:

Epacadostat is a pill that you will take by mouth every 12 hours. You do not need to take it with food, but you can if you want to. If you need to take your Epacadostat earlier than scheduled or

you missed the dose, you can take it up to 4 hours before or after the scheduled time. If more than 4 hours have passed, skip the dose and take your next scheduled dose. You will be given a Patient's Diary to complete for each cycle. In the diary, you will be asked to record the date, time you took the dose and any doses you may have missed. Please bring the diary with you at every study visit.

Since the drug Epacadostat can interact with other medicines, we will check what other medications you are taking. Rarely and if it is safe, you will be asked by your doctor to stop a medicine that may interact with Epacadostat.

Tests that you will have before you start the treatment

- Electrocardiogram (EKG – a record of your heartbeat) to evaluate your heart
- CT scan of bones if necessary
- Blood tests (about 3 teaspoons):
    - Blood test to check your HLA status (only if you do not have results of this test performed any time before this treatment)
    - Blood test to check your endocrine organs (organs that make hormones). These tests will be done in the morning hours (7-9 am) and after fasting for at least 8 hours.

Ongoing Procedures before treatment on the first day of each cycle

- Physical exam and vital signs
- Review of your symptoms and your ability to perform your normal activities
- Blood Tests (about 1 tablespoon at any visit):
    - Routine blood tests to find out if you have low blood counts, the status of your immune system, and if your liver, thyroid, kidneys, and other organs are working well.
    - PSA and testosterone blood test – (every 4 weeks)
    - Blood test to check your organs that make hormones (every 4 weeks starting at cycle 4). These tests will be done in the morning hours (7-9 am) and after fasting for at least 8 hours. If your test was positive before you started the treatment, you will not be tested again.
- Routine urinalysis

Additional Procedures and Visits

- During cycles 1 and 2 you will need to come for additional safety visits on day 8 for:
    - Physical exam and vital signs
    - Review of your symptoms and your ability to perform your normal activities
    - Routine blood tests (about 1.5 teaspoons) to find out if you have low blood counts, the status of your immune system, and if your liver, thyroid, kidneys, and other organs are working well.

  - EKG every 12 weeks to check your heart if you are receiving Epacadostat.
- Imaging Assessments – a CT scan or if you cannot have a CT scan, an MRI, of chest, abdomen and pelvis and a bone scan– every 12 weeks depending on your response to the treatment).

Additional Research tests

In addition to the tests that we will conduct to determine whether you are having side effects or if you are responding to the study therapy, we will also collect blood samples from you for purposes of research only. About 6-8 tablespoons of blood may be collected at any visit. Some of your samples will be sent outside of the NIH for testing, but any information that can be used to identify you will be removed before we send them.

- To measure drug level in your blood, we will collect samples before and immediately after M7824 infusion on Day 1 of cycles 1 and 3. We will also collect a sample before the infusion on Day 1 of cycles 2, 6, and at the time you finish taking the drugs. Additional samples may be collected every 12 weeks after cycle 6.
- To study the effects of therapy on your immune system we will collect samples before treatment on Day 1 of cycles 1, 2, 3, 6, 12 and at the time you finish taking the drugs. Additional samples may be collected every 12 weeks after cycle 12.
- If you are treated with Epacadostat, we will collect blood samples before Epacadostat on Day 1 of cycle 1 and before and 2 hours after Epacadostat treatment on Day 8 of Cycle 2. We will ask you to fast for 8 hours before these samplings.

When you are finished taking the drugs

About 4 – 5 weeks after you have finished taking the study drug, you will be asked to return for a safety follow up visit. At this visit, you will be asked questions about your health, get a physical exam, and undergo blood tests.

If your disease did not get worse, but you finished taking drugs for any other reasons, we will invite you for imaging studies every 3 months. If you are unable to return for these visits, we will call you to ask about your health and any side effects you may have. You will not be scanned if you start new study therapy.

BIRTH CONTROL

If you are the partner of a woman who can become pregnant, you or your partner will need to practice an effective form of birth control before you start study treatment, during study treatment, and for 4 months after the last drug infusion. If you think that your partner is pregnant, you should tell your study doctor or nurse at once.

Effective forms of birth control include:

- abstinence
- intrauterine device (IUD)

- hormonal [birth control pills, injections, or implants]
- tubal ligation
- condoms
- vasectomy

RISKS OR DISCOMFORTS OF PARTICIPATION

If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss

Drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drugs.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having any symptoms.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.

Late side effects of the investigational agents may affect your ability to tolerate subsequent regimens of standard of care chemotherapy.

Below we show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Risks from study therapy

Note: There are treatments for the side effects listed below, and these treatments can often ease side effects. If you experience any of these side effects, treatment will be provided for you.

As a side effect of this experimental therapy, the immune system may target normal tissue. Normal endocrine organs (organs that make hormones) may not work as well leading to tiredness (from low thyroid hormones or adrenal hormones). This may need to be treated by replacement hormones (pills). We will monitor the hormone levels in your blood during the treatment.

M7824

Likely	**Less Likely**
• Fatigue (tiredness or lack of energy) • Nausea • Diarrhea • Constipation • Vomiting • Swelling of your lower legs or hands • Fever • Decreased appetite • Loss of body fluids (dehydration) • Skin growths called keratoacanthomas. These appear as small bumps and have the potential to turn into squamous cell carcinoma skin cancer gradually over time. We work with a dermatologist at the NIH. If you develop a keratoacanthoma while on this study, we will make every attempt to prevent progression to skin cancer. The dermatologist will monitor you regularly and can remove these lesions if indicated. • Rash, blisters, skin discoloration and other skin abnormalities • Bleeding from various organs. This can include nosebleeds, bleeding from your gums, blood in your urine, stool, etc. This bleeding can be life threatening and require you to receive a blood transfusion. If you experience any bleeding please tell the study team immediately. Tell your doctor if	• Chills (feeling cold) • Blood clots that form throughout the body, blocking small blood vessels. Symptoms may include chest pain, shortness of breath, leg pain, problems speaking, or problems moving parts of the body • Easy bruising • Reaction to other drugs such as rash, anaphylaxis, and changes in blood • Infusion-related reaction, including dizziness or fainting (low blood pressure), flushing, rash, fever, shortness of breath or sick to your stomach, or pain at the site of infusion • Back pain • Cancerous growth on the skin that can be removed • Stroke • Slow wound healing. If you are having surgery, please discuss with your doctor. • Thickening of the skin, nails

you've had a life-long problem of frequent or excessive bleeding or bruising, or if you take aspirin or prescription medication to thin your blood. • Shortness of breath • Cough • Anemia- low number of red blood cells that can cause tiredness and shortness of breath. May require a transfusion • Abdominal pain • Headache • Itching	

Allergic reactions or reactions in the context with the infusions might occur during treatment. Although M7824 is a fully human protein the risk cannot be completely excluded. In general, these reactions are mild to moderate and can be handled with appropriate drugs, but in very rare cases severe to life-threatening and even fatal reactions might occur, which require advanced cardiac life support.

In addition to the above, we have seen a few cases of nodular regenerative hyperplasia. This is when small growths, or nodules, occur in the liver. These usually do not cause symptoms, but can occasionally be associated with high blood pressure in the vein to the liver which could over time lead to liver damage.

In addition, immune-mediated side effects might be possible. These side effects are caused by over activity of your body's immune system. The immune system normally works to protect you from things that are harmful such as infections, foreign substances, and sometimes from cancer. If the immune system is overactive, it can attack normal parts of the body because it mistakenly recognizes them as foreign/harmful.

Examples of these side effects are listed below. In rare cases, immune-related side effects can be life-threatening or fatal.

- joint pain
- arthritis (inflammatory disease of the joint)
- pneumonitis (inflammatory disease of the lung): symptoms may include but are not limited to a new or worsening cough, shortness of breath possibly with fever. Preliminary data suggested that there may be the tendency of higher frequency and severity in Japanese patients compared with non-Japanese patients: tell your study doctor right away if you have any of these symptoms as it may need to be treated urgently
- hypothyroidism (decreased function of the thyroid gland)
- hyperthyroidism (increased function of thyroid gland)

- thyroiditis (inflammatory disease of the thyroid gland)
- autoimmune hepatitis (inflammatory disease of the liver caused by the body's immune system): Signs and symptoms of this include yellowing of the skin or whites of the eyes, dark urine, severe nausea and vomiting, pain in the upper right side of your abdomen, skin itchiness, not feeling hungry and bleeding or bruising more easily than normal
- thrombocytopenia (decrease of the blood platelets)
- inflammatory eye disease (Uveitis)
- diabetes mellitus (high blood sugar levels)
- decreased function of the adrenal glands or other glands that produce important hormones. This may cause stomach pains, vomiting, muscle weakness and fatigue, depression, low blood pressure, weight loss, kidney problems, and changes in mood and personality. These complications may be permanent and may require hormone replacement. If this occurs, medication can effectively treat this.
    - Since this condition could occur months after receiving immunotherapy, it is important that you tell your outside doctor that you were on an immunotherapy if you experience decreased energy, headaches, persistent nausea/vomiting, or dizziness after you are done with your NIH follow up period.
- inflammatory disease of muscles characterized by pain and tenderness
- colitis (inflammatory disease of the large intestine): It may cause abdominal pain and diarrhea with or without blood. Fever may be present. It may require you to receive additional fluids. If left untreated, in rare occasions this may lead to a tear in the wall of the intestine which can be serious and life threatening
- impairment of the brain function
- nerve irritation that can result in pain, numbness and/or weakness in any part of the body. In rare situations, there is the potential for the nervous system to be severe.
- skin rash with blisters that can be itchy
- myocarditis (inflammation of the heart muscle)
- kidney problems: you may have an increase of creatinine levels in a blood test (creatinine is a protein marker that measures kidney function) but not have any symptoms or feel unwell. Uncommonly a patient may experience nephritis which is an inflammation of the kidneys that stops the kidneys from working properly
- problems with the pituitary gland (hypopituitarism): Hypopituitarism refers to decreased output of hormones from the pituitary gland in the brain and may be caused by inflammation of the pituitary gland (hypophysitis). Symptoms may include headaches, thirstiness, and trouble seeing or double vision, leakage of breast milk or irregular periods in women. These complications may be permanent and may require hormone replacement
- pancreatitis (inflammation of the pancreas)
- liver problems: Increases in the blood level of substances called enzymes found within your liver cells. The enzyme changes are unlikely to make you feel unwell, however, if

these blood enzyme levels become very high, your study doctor may need to stop the study medication

- Nervous system problems: symptoms can include unusual weakness of legs, arms, or face, numbness, or tingling in hands or feet. In rare situations, there is the potential for the inflammation of the nervous system to be severe.

If any of these side effects occur, you must inform your study doctor immediately.

BN-brachyury vaccine

Likely	**Less Likely**	**Rare but Serious**
• Injection-site reaction (pain or discomfort, itching, redness, firmness, swelling, skin thickening, or bumps)	• Acute fever • Chills • Flu-like symptoms (fatigue, soreness, general body pain, abdominal pain, cough, fever, headache) • Chest tightness • Shortness of breath • Leg pain and/or swelling • Headache • Loss of appetite • Weight loss • Diarrhea • Constipation • Rash • Nausea • Dizziness • Mild inflammation of tissue lining the lungs • Chronic inflammation of the skin • Difficulty sleeping • Open sores (ulcers) at the injection site • Enlarged lymph nodes • Low blood levels of sodium • Inflammation of the testicles • Inflammation of thyroid tissue	• Difficulty breathing • Low blood pressure • Wheezing • Clots in the lung • Clots in the leg • Kidney damage • Decreased blood oxygen levels • Fluid around the lining of the lungs • Fluid around the lining of the heart

N-803 (previously known as ALT-803)

Common (out of 100 people who receive N-803, 20 or more people may have):

- Feeling tired
- Fever and chills
- Flu-like symptoms
- Headache
- High blood pressure
- Low blood pressure
- Large red rash and/or swelling at the site of injection that fades over 1-2 weeks (out of 100 people, 50 or more people may have this)
- Abdominal pain
- Low albumin, which may cause fluid build-up, yellowing of your skin, rapid heart beat, nausea and vomiting, itchy skin or appetite changes
- Back pain

One or more of these side effects may begin 1-2 days after receiving N-803 and go away a few days later.

Uncommon *(*out of 100 people who receive N-803, 1 or less people may have):

- Low white blood cell counts
- Atrial fibrillation, a quivering or irregular heartbeat (arrhythmia), that can lead to blood clots, stroke, heart failure and other heart-related complication and may require the addition of a blood thinner

Epacadostat

Likely	Less Likely	Rare but Serious
• Diarrhea • Nausea • Vomiting • Fatigue/general weakness • Rash	• Abnormal liver tests • Joint pains • Itching • Decreased thyroid function	• Adrenal insufficiency, a condition in which the glands on top of the kidneys do not make enough of a hormone. This can cause tiredness, weakness, feeling faint, salt craving, and in severe cases require hospitalization or be life threatening if not treated promptly. • Serotonin syndrome (SS) is a rare condition associated with certain types of medications. SS can be mild or life-threatening. People with Serotonin Syndrome may experience a feeling

Likely	Less Likely	Rare but Serious
		that their heart is racing, confusion, fever, chills, sweats, muscle spasms, stomach upset, or seizures. Rarely, patients taking Epacadostat have experienced mild or moderate symptoms that might have been Serotonin Syndrome. A patient card discussing the SS will be provided to you by the study doctor.

Risks of Epacadostat when combined with M7824

Likely	Less Likely	Rare but Serious
• Fatigue • Nausea • Diarrhea • Rash • Vomiting • Fever, Abdominal pain • Aspartate aminotransferase and Alanine aminotransferase increased (Liver enzymes increased) • Weakness	• Muscle pain • Pneumonia • Inflammatory disease of the lung/intestine • Adrenal insufficiency (Hormonal disorder)	• Drug sensitivity • Inflammation of the brain • Drug reaction with eosinophilia (increased number of these blood cells) • Systemic symptoms, and immune-mediated hepatitis

More than one of these side effects may happen at the same time. If you experience any of these symptoms, follow the instructions provided by your study doctor.

Risks from Blood Collection

Side effects of blood draws include pain and bruising in the area where the needle was placed, lightheadedness, and rarely, fainting. When large amounts of blood are collected, low red blood cell count (anemia) can develop.

What are the risks of radiation from being in the study?

During your participation in this research study, you will be exposed to radiation from up to 5 CT scans (chest/abdomen/pelvis) and up to 5 bone scans annually. The amount of radiation exposure you will receive from these procedures is equal to approximately 7 rem (or 7.45 rem if you weigh more than 265 lb). A rem is a unit of absorbed radiation.

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. The average person in the United States receives a radiation exposure

of 0.3 rem per year from these sources. This type of radiation is called "background radiation." No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The CT and bone scans that you get in this study will expose you to the roughly the same amount of radiation as 23years (or 24.8years if you weigh more than 265 lb) of background radiation. Being exposed to too much radiation can cause harmful side effects such as an increase in the risk of cancer. The risk depends on how much radiation you are exposed to. Please be aware that about 40 out of 100 people (40%) will get cancer during their lifetime, and 20 out of 100 (20%) will die from cancer. The risk of getting cancer from the radiation exposure in this study is 0.7 out of 100 (0.7%) and of getting a fatal cancer is 0.4 out of 100 (0.4%).

Risks due to Contrast dye used in CT scans

If contrast dye is used, there is a risk for allergic reaction to the dye. If you are allergic to or sensitive to medications, contrast dye, iodine, or shellfish, you should notify it to the Study team. If you have had kidney problems/failure in the past, please notify it to your study doctor.

Risks of Bone Scan

The bone scan carries no greater risk than conventional X-rays. The tracers in the radioactive substance used in a bone scan produces very little radiation exposure. The risk of having an allergic reaction to the tracers is low.

Risks of MRI

MRI is safe and there are no side effects. People who have some kinds of metal in their body are at risk for injury from the MRI magnet. You will be questioned about having metal in your body before your MRI and you will not have the MRI if it is determined that is not safe to do so. It may be unsafe for you to have an MRI scan if you have pacemakers or other implanted electrical devices, brain stimulators, some types of dental implants, aneurysm clips (metal clips on the wall of a large artery), metal prostheses (including metal pins and rods, heart valves, and cochlear implants), permanent eyeliner, tattoos, an implanted delivery pump, or shrapnel fragments. Welders and metal workers may have small metal fragments in the eye. You will be screened for these conditions before having any MRI scan. If you have a question about metal in your body, you should inform the staff. You will be asked to complete an MRI screening form before each MRI scan you have.

In addition, all magnetic objects (like watches, coins, jewelry, and credit cards) must be removed before entering the MRI scan room.

People with fear of confined spaces may become anxious during an MRI. Those with back problems may have back pain or discomfort from lying in the scanner. The noise from the scanner is loud enough to damage hearing, especially in people who already have hearing loss. Everyone having a research MRI scan will be fitted with hearing protection. If the hearing protection comes loose during the scan, you should let us know right away.

There are no known long-term risks of MRI scans.

Risks of Gadolinium- a contrast dye used in MRIs

The risks of an IV catheter include bleeding, infection, or inflammation of the skin and vein with pain and swelling.

Mild symptoms from gadolinium infusion occur in fewer than 1% of those who receive it and usually go away quickly. Mild symptoms may include coldness in the arm during the injection, a metallic taste, headache, and nausea. In an extremely small number, fewer than one in 300,000 people, more severe symptoms have been reported including shortness of breath, wheezing, hives, and lowering of blood pressure. You should not receive gadolinium if you previously had an allergic reaction to it. You will be asked about such allergic reactions before gadolinium is given.

People with kidney disease are at risk for a serious reaction to gadolinium contrast called "nephrogenic systemic fibrosis (NSF)". This condition always involves the skin and can also involve the muscles, joints and internal organs. NSF has resulted in a very small number of deaths. A blood test of your kidney function may be done within the month before an MRI scan with gadolinium contrast. You will not receive gadolinium for a research MRI scan if your kidney function is below the safe level.

Most of the gadolinium contrast leaves the body in the urine. However, the FDA has issued a safety alert that indicates small amounts of gadolinium may remain in the body for months to years. The long-term effects of the retained gadolinium are unknown. Some types of gadolinium contrast drugs are less likely to remain in the body than others. In this study, we will use the gadolinium contrast drugs that are less likely to remain in the body.

Risks of Biopsy

There are potential risks associated with this procedure including pain or bleeding caused by the anesthesia needle as well as the biopsy procedure itself. An allergic reaction to the local anesthetic may occur. There may be bruising at the site of biopsy. Continuous bleeding and infection are rare and very often is easily controlled.

Risks due to Electrocardiogram (EKG)

Other than possibly experiencing some minor skin irritation from the electrodes, there are no anticipated risks related to complete the electrocardiogram and/or the echocardiogram.

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

The aim of this study is to find out whether the experimental treatment will cause your tumors to shrink. We do not know if you will receive personal, medical benefit from taking part in this study. Potential benefits could include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer. Because there is not much information about the drug's effect on your cancer, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

ALTERNATIVE APPROACHES OR TREATMENTS

Instead of being in this study, you have these options:

- Getting treatment or care for your cancer without being in a study
  - If you have prostate cancer, enzalutamide, abiraterone acetate and docetaxel are three other types of treatments that can make men with CRPC live longer.
  - If you have another type of cancer, ask your doctor if an alternative treatment is appropriate for you.
- 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. It does not treat the cancer directly. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Please talk to your doctor about these and other options.

STOPPING THERAPY

Your doctor may decide to stop your therapy for the following reasons:

- if he/she believes that it is in your best interest
- if your disease comes back during treatment
- if you need to take medication that is not allowed on the study
- if you have side effects from the treatment that your doctor thinks are too severe
- if new information shows that another treatment would be better for you
- if the investigator decides to end the study

In this case, you will be informed of the reason therapy is being stopped.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to EMD Serono, Bavarian Nordic, Inc., Immunity Bio, Incyte or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases can**not** be recalled and destroyed.

CONFLICT OF INTEREST

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a COI Guide. You may ask your research team for a copy of the COI Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines or the guidelines of their home institution, but they do not need to report their personal finances to the NIH.

The National Institutes of Health and the research team for this study are using therapies developed by EMD Serono, Immunity Bio, Bavarian Nordic, Inc, and Incyte through a joint study with your researchers and the companies. The company also provides financial support for this study.

USE OF SPECIMENS AND DATA FOR FUTURE RESEARCH

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

These specimens and data will be used for future research and shared with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that they may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. Someone will work with you to provide more information.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- If some tests and procedures performed outside the NIH Clinical Center, you may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- Qualified representatives from the pharmaceutical companies, producing drugs: EMD Serono (M7824), Immunity Bio (N-803), Bavarian Nordic, Inc (BN-Brachyury), Incyte (Epacadostat).

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, James Gulley, MD, PhD, Phone: 301-480-7164, Email: gulleyj@mail.nih.gov. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR	Print Name of LAR	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness should sign below if either:

1. **A short form consent process has been used to enroll a non-English speaking subject or**
2. **An oral presentation of the full consent has been used to enroll a blind or illiterate subject:**

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.