Medical University of South Carolina
CONSENT TO BE A RESEARCH SUBJECT

TITLE OF RESEARCH:
A Phase II Trial of Adjuvant PROSTVAC-V/F in Subjects at High Risk for Relapse after Radical Prostatectomy

MUSC CTO 102377
NCT02772562
MUSC PI: Dr. Michael Lilly

A. PURPOSE OF THE RESEARCH

You are being asked to volunteer for a research study. Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As the study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand.

The study drug being looked at for this study is PROSTVAC-V/F. PROSTVAC-V/F is a PSA-Targeted Immunotherapy product that may help cells from your own body to recognize and kill the cancer cells. PROSTVAC-V/F teaches the immune system (group of cells and organs in the body that recognize and fight infection) to find and kill certain cancer cells, in this case prostate cancer cells. You are being asked to volunteer for this study because you have recently had a prostatectomy and are at high risk for relapse of prostate cancer.

The purpose of this study is to see how well PROSTVAC –V/F works in stopping prostate cancer from coming back or relapsing. This study will also look at the safety of PROSTVAC-V/F. This is an investigational vaccine regimen, which means that it is not approved by the Food and Drug Administration (FDA) and can be used only in a research study.

PROSTVAC-V/F has two parts, PROSTVAC-V and PROSTVAC-F. PROSTVAC-V is made from vaccinia virus that was used for many years to vaccinate against smallpox. PROSTVAC-F is made from fowlpox virus. This virus is a relative of vaccinia virus but is found only in birds and does not cause any human disease. Both viruses have four genes added to them. One of these genes is the gene for PSA – a human protein that is also produced by prostate cancer cells. The other three genes are for three molecules (which together are called TRICOM™) which can increase the body's immune response to the vaccine.

The study is sponsored by the Medical University of South Carolina (MUSC). The investigator in charge of this study is Dr. Michael Lilly. Bavarian Nordic, Inc. (BNI) is supplying the drug PROSTVAC-V/F. BNI is also providing payments to MUSC and Dr. Lilly to support activities that are required to conduct and manage the study. No one on the research team will receive a direct payment or an increase in salary for conducting the study.

About 30 people will be enrolled study-wide with about 25 patients being enrolled at MUSC under the direction of Dr. Michael Lilly.

B. PROCEDURES

If you agree to be in this study, the following will happen:

Before you begin the study

You will need to have the following exams, tests or procedures to find out if you can be in the study. These exams, tests or procedures are part of regular 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 the study doctor. It may take about 3 hours to complete *all* of the tests below.

- History and physical exam. The study doctor will also review any medications you are taking.
- About 3 teaspoons (or 15 milliliters (mL)) of blood will be taken to look at your blood counts, the health of your kidneys and liver, to look at your prostate health and your electrolyte balance. Electrolytes are minerals in your blood that help maintain your body's blood chemistry, muscle action and other bodily functions. You will also have a hepatitis B, hepatitis C and HIV screening (if not done in the last 2 years). You will need to fast for 12 hours before the blood draw.
- Radiographic scans using Computed Tomography (CT) and bone scan. These scans will give a detailed picture of the areas of the body taken from different angles.

  A CT scan is a way to make x-ray images of the inside of the body. The CT scanner is a doughnut-shaped machine that uses x-rays to create computer pictures that show structures inside your body more clearly than regular x-ray pictures. During the procedure, a technologist will take you into the CT scan room where you will lie down on the patient table (usually on your back) inside of the CT machine. You should get comfortable because it is very important not to move during certain parts of the test.

  CT examinations differ depending on the part of your body being studied. For example, if your abdomen is being studied, a series of pictures will be taken from your lower chest to your lower pelvis. During the study, you will be asked to hold your breath so that the pictures will not be blurred. The machine will make some noise, and the table will move during the scan. Also, you may receive signals from the technologist or from the machine about your breathing. Before or during the study, you may be given an injection of a contrast liquid in your vein to allow the radiologist to obtain clearer images of your organs. If you have any discomfort during the test or after the injection, be sure to tell the technologist. If the study doctor finds that you do not meet the specific eligibility requirements to be in this study, you will not be able to participate. You will continue to see your regular doctor who will discuss with you additional options for your disease.

A bone scan involves injecting a small amount of radioactive material (radiotracer) into a vein. The substance travels through your blood to the bones and organs. As it wears off, it gives off a little bit of radiation. This radiation is detected by a camera that slowly scans your body. The camera takes pictures of how much radiotracer collects in the bones.

You will also have the following research procedures before you start study drug:

- Questionnaires asking about your quality of life and how you are feeling.
- About 9 teaspoons (about 45 mL) of blood will be collected to look at tumor markers and antibodies that may be in your body when you have cancer. Studying these markers and antibodies in the blood may help researchers learn more about this type of cancer in the future. Researchers will also look at genetic markers and your DNA for genetic research.

  DNA is short for deoxyribonucleic acid. DNA contains information that determines in part the traits, such as eye color, height, or disease risk, that are passed on from parent to child. Genetic research is research done to identify genes that cause or contribute to a disease or trait. It is an increasingly important way to try to understand the role of genes in human disease.
- We will look at the leftover tissue (tissue not used for your diagnosis) from your original biopsy or surgery to see what genetic mutations may be in your tumor. This will help us see if there is a difference in how your tumor responds based on the mutation in the tumor.
- A research assistant from MUSC will contact you over the phone or will see you in clinic to review a life-experiences questionnaire. This questionnaire will ask questions about your general health, feelings about your cancer diagnosis, social relationships, thoughts about prostate cancer recurrence and live events from the last year. It should take about 30 minutes to complete.

If the exams, tests and procedures show that you can be in the study, and you choose to take part, then you will be registered to the study and will begin study participation. If the study doctor finds that you are not eligible for this study, you will not be able to participate. You will continue to see your regular doctor who will discuss with you additional options for your disease

While you are receiving study drug:

After you have been registered to the study, you will follow the schedule of procedures below. Depending on clinic schedules, each visit may take about 3 hours to complete. The history and physical exam and blood tests described are part of your regular cancer care.

Day 1:

- History and physical exam. The study doctor will also ask you about any medications you are taking

- About 2 teaspoons (about 10mL) of blood will be taken to look at your blood counts, the health of your kidneys and liver and to look at your electrolyte balance.
- You will get the first part of the study drug, PROSTVAC-V. This drug is given by subcutaneous injection (a needle is put under your skin). You will get a 0.5mL dose of PROSTVAC-V. This is the only dose of PROSTVAC-V that you will get.
- At this visit, a study nurse will give you supplies to take care of the vaccination site. The supplies will include bandages, disposable gloves, absorbent toweling or gauze, instructions for caring for the injection site, special bags for disposing of used bandages, and contact information for the study staff. You will need to follow the instructions that you are given in order to ensure your injection site heals properly.

Days 15, 29, 57, 85, 113 and 141:

- History and physical exam. The study doctor will also ask you about any medications you are taking or any side effects you may be having.
- About 2 teaspoons (or 10mL) of blood will be taken to look at your blood counts, the health of your kidneys and liver and to look at your electrolyte balance
- You will get the second part of the study drug, PROSTVAC-F. This drug is given by subcutaneous injection (a needle is put under your skin). You will get a 0.5mL dose of PROSTVAC-F.

On Day 85 you will also have the following research procedures:

- About 9 teaspoons (about 45 mL) of blood will be collected to look at tumor markers and antibodies that may be in your body when you have cancer.
- Questionnaires asking about your quality of life and how you are feeling.

During Follow Up:

After your last dose of study drug (day 141), you will enter the follow up part of the study. You will be asked to return to the clinic every twelve weeks for follow up tests. Depending on clinic schedules, each visit may take about 3 hours to complete. These tests are part of your regular cancer care.

- History and physical exam. The study doctor will also ask you about any medications you are taking or any side effects you may be having.
- About 2 teaspoons (or 10mL) of blood will be taken to look at your blood counts, the health of your kidneys and liver, to look at your electrolyte balance and your prostate health

About three months after your last dose of study drug (Day 225) and at the end of the follow up period (Day 730), you will have the following research assessments. These are not part of your regular cancer care:

- Questionnaires asking about your quality of life how you are feeling
- About 9 teaspoons (or 45 mL) of blood will be collected to look at tumor markers and antibodies that may be in your body when you have cancer.

Withdrawal

Taking part in this study is voluntary. You do not have to be in this research study. You can agree to be in the study now and change your mind later. You may discontinue your study participation at any time. Your decision will not affect your regular care. It will not affect your getting all the care, medicine, and equipment you should be getting.

The study doctor, BNI or the FDA can take you out of the study at any time with or without your agreement. These decisions will be made if:

- It is in your best medical interests to stop your participation.
- You do not follow instructions.
- The study is canceled.

The doctor will explain the reasons for doing so and will help arrange for your continued care by your own doctor, if needed. If you leave the study for any reason, you will be asked to have the procedures completed for the final visit.

If you want to withdraw from the study, contact Dr. Michael Lilly at (843) 792-4271. If you withdraw after you have started in the study, the study staff and the study doctor will stop collecting your health information. Although they will stop collecting new information about you, they will need to use the information they have already collected to evaluate the study results. If you start the study and then cancel your permission, you will not be able to continue to participate in the study or receive any drug as part of the study. This is because the study staff and/or the study doctor would not be able to collect the information needed to evaluate the study drug.

C. DURATION

Each study visit will take about 3 hours, depending on the clinic schedule.

Participation in the study will take about 15 visits over a period of 24 months. You will receive study drug over a period of 5 months and be in follow up for about 19 months.

You can stop participating in the study at any time for any reason.

D. RISKS AND DISCOMFORTS

While on this study, you are at risk for the side effects listed below. Not

everyone will get these side effects. You may have none or several. Most people do not experience all of the side effects listed. A side effect may get worse while on study drug, or more side effects may develop as the longer you stay on study. This depends on your general health and the amount of the study drug you receive (the dose).

Care will be taken to minimize adverse reactions, but unexpected or unanticipated adverse effects that could be severe or fatal are possible. While on this study, you will be monitored for all adverse effects and will be treated with appropriate medical care if they occur.

PROSTVAC V/F

Most Common (greater than or equal to 50% of subjects):

- Injection site reactions including skin reddening, itching, hardening and swelling

Common (greater than or equal to 10% of subjects):

- Headache
- Fatigue (extreme tiredness)
- Muscle pain
- Nausea

The following events have been reported in studies using PROSTVAC-V/F but how often these events occur is unknown:

- Fever
- Pain at the injection site
- Chills
- Swelling in the lower part of the body
- Dizziness
- Flu-like symptoms

Vaccinia Virus

PROSTVAC-V/F is made up of two parts. PROSTVAC-V is made from vaccinia virus that was used for many years to vaccinate against smallpox.

This section describes the risks of the vaccinia virus.

Contact Transmission

A potential problem associated with PROSTVAC-V is accidental spread of the virus to another area of your body. You can transfer the virus to your eye and mucous membranes (inner lining) of the nose or mouth by scratching the vaccination site and then rubbing the eye or an open skin area. If you participate in this study, you will have to take special care of your vaccination site and wash your hands often to prevent spreading of the virus. You will be provided with written instructions, which will provide details about the vaccination site and how to care for it, as well as how to contact the study staff if you have

questions or concerns. **If a lesions appears somewhere other than the original injection site, contact the study team immediately.** The lesion may be tested and you may have to take special precautions until the results of the test are known.

Because you may "shed" live virus from the vaccination site after vaccination until the vaccination site heals completely, and could spread the virus to others, you must avoid close contact with the following people until your injection site heals completely. This is only required after your first injection.

- People with weak or suppressed immune systems such as individuals with leukemia or lymphoma, individuals with AIDS, or those receiving treatment to suppress their immune system (for example, after organ transplantation);
- people with eczema or other significant skin rashes, itching infections, burns, chicken pox, or skin injury;
- women who are pregnant or breast-feeding; or
- children under 3 years of age

"Close contact" means that these people share your house with you, are in physical contact with you, come in contact with your bed linens or clothes, and/or you take care of them and touch them.

Rare but serious reactions associated with vaccinia virus

- Generalized vaccinia: a lesion (an injury or wound) to the skin that may occur after the vaccination.
- Progressive vaccinia: condition where the vaccination site does not heal but expands causing tissue death. If not treated, there may be severe complications including shock and other severe infections, which could lead to death.
- A condition called eczema vaccinatum with symptoms of crusting skin rashes on the face, neck, chest, abdomen, upper limbs and hands. Other symptoms include fever and facial edema. The condition may be fatal if severe and left untreated.
- Inflammation of the brain after injection that can cause flu-like symptoms, confusion, seizures or problems with senses r movement. Severe cases of this inflammation can be life threatening.
- A buildup of fluid in the heart.
- Smallpox infection in the eye.

None of these side effects have been seen in subjects treated with PROSTVAC-V.

If you develop any of these side effects, a treatment called Vaccinia Immune Globulin (VIG) may be used. VIG has been approved by the FDA to treat people who have complications from exposure to vaccinia.

Fowlpox Virus

PROSTVAC-F is based on fowlpox virus. The fowlpox virus naturally infects birds has been studied and used in other vaccines for at least twenty years. The virus does not grow (replicate) in human cells and does not infect humans or cause human disease. The vaccines including fowlpox virus have been given in research studies to both animals and humans for HIV, malaria and cancer. Side effects from fowlpox are mild and could include injection site reactions, fever, fatigue, low red blood cell count and low white blood cell count. With any experimental compound, there is the risk of unexpected and serious or deadly complications, even if these side effects have not been seen before.

Other Potential Side Effects

Additional adverse effects may be related to the immune response to the PSA and/or proteins that are part of the vaccines. Some normal human cells (such as normal prostate cells) have these proteins on their surface. If the vaccine causes an immune reaction against these normal cells, you could develop swelling or inflammation of these tissues. While unlikely, it is also possible that if you develop a very active antibody (immune) reaction after the vaccination, you could develop an immune complex disease (or serum sickness) which can cause fevers, rashes, joint pains, and less commonly, kidney failure and severe allergic reaction inside blood vessels (vasculitis) or any part of your body. Over 1500 subjects have participated in clinical studies of PROSTVAC-V/F. None of these symptoms have been seen to date in the subjects receiving PROSTVAC-V/F, but they could occur.

Genetic Research

Genetic research studies may present unique risks to human subjects and their relatives. These involve medical, psychosocial and economic risks, such as the possible loss of confidentiality (private information), loss of insurability and employability, paternity, and social stigmas. Knowledge of one's genetic make-up may also affect one's knowledge of the disease risk status of family members. Genetic research raises difficult questions about informing you and other subjects of any results, or of future results. Some people feel anxious about the possibility of having a defective gene that would place them or their children at risk. Some people want to know what is found out about them; others do not. The risks of knowing include anxiety and other psychological distress. The risks of not knowing what is found include not being aware if there is treatment for the problem being studied. But these risks can change depending on whether there is a treatment or cure for a particular disease and on how clear the results are. If there is a medical reason to seek specific information from you, your doctor will tell you this. A process called "genetic counseling" is often appropriate in such cases; you should ask your doctor or nurse about this if you have any questions.

South Carolina law, mandates that your genetic information obtained from any test or from this research, be kept confidential. Our state law prohibits an insurer using this information in a discriminatory manner against your or any of your family in issuing or renewing insurance coverage for you or your family. Our state law further prohibits our sharing your genetic information with anyone except in a few narrow circumstances, one of these being a research project of this type, approved by the

Institutional Review Board and then we must take all steps to protect your identity. You will still be responsible for paying for health care, however. The Medical University of South Carolina will not be responsible for such costs, even if care is needed for a condition revealed during research or clinical testing.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this new federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance, nor does it protect you against genetic discrimination by all employers.

Hepatitis and HIV screening:
Per South Carolina law, if you test positive for Hepatitis B, Hepatitis C, or HIV the results of your test must be reported to the South Carolina Department of Health and Environmental Control.

Pregnancy Risks
PROSTVAC-V/F has not been studied in pregnant women, so the risks to unborn fetuses is not known.

Risks/Side Effects from Blood Draws
Risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting is possible, although unlikely. The person drawing your blood will attempt to minimize this discomfort.

CT Scan
The CT scan used to measure the tumor size will expose you to some radiation. Although the radiation from each scan is within acceptable limits, these exposures add up over one's life. The amount of radiation, you will be exposed to is relatively small. Such doses of radiation may be potentially harmful, but the risks are so small that they are difficult to measure. If you have already had many x-rays, you should discuss this with the researchers before agreeing to be in the study.

A contrast dye may be used in order to help your organs show up in the scan. If used, the contrast dye will be injected into your vein to assist the study doctor and site staff in viewing the scan. One rare risk associated with contrast dyes include excessive scarring of the skin tissue, joints, eyes and internal organs. Such scarring is called nephrogenic systemic fibrosis and is particularly hazardous for people with pre-existing kidney problems. Other uncommon risks include itching or irritation at the injection site and possible allergic reactions. The study doctor will discuss this with you.

Bone Scan

Bone scans are commonly performed and considered safe. During the scan, you are exposed to a very low amount of radiation. The amount of radiation is less than one tenth of the amount used during a normal chest X-ray and equivalent to one day of exposure to natural background radiation. The amount of radiation used during a DXA scan is considered safe for adults but can cause damage to unborn babies.

Loss of confidentiality

There is a risk of loss of confidentiality since medical records will be reviewed during this study.

Unknown risks

The experimental study drug may have unknown side effects. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

E. BENEFITS

If you agree to take part in this study, there may or may not be direct medical benefit to you. Your participation in this study may provide important information regarding the study drug and that may lead to future clinical studies. Other patients with cancer may benefit in the future.

F. COSTS

You and/or your insurance company will be billed for the clinic visits, all standard laboratory tests (e.g. routine blood counts and blood chemistry tests) and CT and bone scans. Some health plans will not pay these costs for people taking part in studies. Check with your insurance company to find out what they will pay for, as if they refuse to pay you will be held financially responsible.

The drug PROSTVAC-V/F will be supplied free of charge by BNI. The following procedures are not considered standard of care and will be paid for by the sponsor:

- Blood samples to look at your tumor markers and questionnaires for research purposes
- Hepatitis B, Hepatitis C, and HIV testing
- Lipid panel

Please ask Dr. Michael Lilly if you would like to know more about which tests and studies are being done solely for research purposes.

G. PAYMENT TO PARTICIPANTS

In return for your time, you will be given $20 cash at screening, at Day 85, at Day 225 and at Day 730, for a total of $80. If you live 100 miles or more from the cancer center, you will be given an additional $30 cash for each visit for a total of $200. This extra amount is for travel reimbursement.

In return for your time and effort for completing the life-experiences questionnaire, you will be given $15 gift card. If this questionnaire is completed over the phone, this gift card will be mailed to you after the call, once your address has been confirmed.

Payments that you receive from MUSC for participating in a research study are considered taxable income per IRS regulations. Payment types may include, but are not limited to: checks, cash, gift certificates/cards, personal property, and other items of value. If the total amount of payment you receive from MUSC reaches or exceeds $600.00 in a calendar year, you will be issued a Form 1099.

H. ALTERNATIVES

If you choose not to take part in this study, the usual or standard choices for treatment for your stage of cancer may include

- supportive care only (no treatment such as chemotherapy or radiation),
- treatment with different drugs or drug/radiation combinations, or
- other experimental treatments

If you choose to participate in this study, you will be able to receive standard treatments during the follow up part of the study. Your participation in this study may prevent you from participating in other studies of experimental treatments, if those studies do not allow subjects who have previously received viral therapy. Your doctor will discuss these alternative treatments with you, including the benefits and risks involved. Your doctor will also keep you informed of any new treatment options that become available during the course of your participation in this study.

I. SIGNIFICANT NEW FINDINGS

If there are significant new findings during the course of the study, you will be notified.

J. STUDENT PARTICIPATION

Your participation or discontinuance will not constitute an element of your academic performance, nor will it be a part of your academic record at this Institution.

K. EMPLOYEE PARTICIPATION

Your participation or discontinuance will not constitute an element of your job performance or evaluation, nor will it be a part of your personnel record at this Institution.

L. CLINICAL TRIALS.GOV

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.

M. SPONSOR COMMITMENT

In the event of a study related injury, MUSC will provide medical treatment to you. MUSC will bill your insurance company, however should the insurance company deny coverage or if insurance is not available, you will be responsible for payment of services.

N. FUTURE CONTACT

The researcher in charge of this study might like to contact you in the future about other research opportunities. Please initial by your choice below:

____Yes, I agree to be contacted about future research opportunities

____No, I do not agree to be contacted about future research opportunities.

Results of this research will be used for the purposes described in this study. This information may be published, but you will not be identified. Information that is obtained concerning this research that can be identified with you will remain confidential to the extent possible within State and Federal law. The sponsor and the Food and Drug Administration (FDA) will receive copies of the research records. The investigators associated with this study, employees of the sponsor, the FDA, and the MUSC Institutional Review Board for Human Research will have access to identifying information. All records in South Carolina are subject to subpoena by a court of law.

In the event of a study related injury, you should immediately go to the emergency room of the Medical University Hospital, or in case of an

emergency go to the nearest hospital, and tell the physician on call that you are in a research study. They will call the study doctor who will make arrangements for your treatment. If the study sponsor does not pay for your treatment, the Medical University Hospital and the physicians who render treatment to you will bill your insurance company. If your insurance company denies coverage or insurance is not available, you will be responsible for payment for all services rendered to you.

Your participation in this study is voluntary. You may refuse to take part in or stop taking part in this study at any time. You should call the investigator in charge of this study if you decide to do this. The data collected on you to this point remains part of the study database and may not be removed. Your decision not to take part in the study will not affect your current or future medical care or any benefits to which you are entitled.

The investigators and/or the sponsor may stop your participation in this study at any time if they decide it is in your best interest. They may also do this if you do not follow the investigator's instructions.

Volunteers Statement

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. If I have any more questions about my participation in this study or study related injury, I may contact Dr. Michael Lilly at (843) 792-4271. I may contact the Medical University of SC Hospital Medical Director (843) 792-9537 concerning medical treatment. If I have any questions, problems, or concerns, desire further information or wish to offer input, I may contact the Medical University of SC Institutional Review Board for Human Research IRB Manager or the Office of Research Integrity Director at (843) 792-4148. This includes any questions about my rights as a research subject in this study.

I agree to participate in this study. I have been given a copy of this form for my own records.

If you wish to participate, you should sign below.

Signature of Person Obtaining Consent	Date	Signature of Participant	Date