MC200710 / 21-006302

Stimulating Immune Response with Neoadjuvant Human Papilloma Virus (HPV)-16 specific Vaccination in HPV-Oropharyngeal Squamous Cell Carcinoma (HPV-OPSCC)

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RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: MC200710 Stimulating Immune Response with Neoadjuvant Human Papilloma Virus (HPV)-16 specific Vaccination in HPV-Oropharyngeal Squamous Cell Carcinoma (HPV-OPSCC)

IRB#: 21-006302

Principal Investigator: David M. Routman, M.D., and Colleagues

Key Study Information

This section provides a brief summary of the study. It is important for you to understand why the research is being done and what it will involve before you decide. **Please take the time to read the entire consent form carefully and talk to a member of the research team before making your decision.** You should not sign this form if you have any questions that have not been answered.

It's Your Choice	This is a research study. Being in this research study is your choice; you do not have to participate. If you decide to join, you can still stop at any time. You should only participate if you want to do so. You will not lose any services, benefits, or rights you would normally have if you choose not to take part.
Research Purpose	The purpose of this study is to test an investigational vaccine called PDS0101 or the combination of PDS0101 plus pembrolizumab for the treatment of high-risk head and neck cancer. You have been asked to take part in this research because you have been diagnosed with head and neck cancer that is considered to be at a higher risk of recurrence and you are planning to have surgery to remove the cancer and radiation therapy or chemotherapy and radiation therapy.

What's Involved	Study participation involves four to six visits, some of which will be on the same days you will have appointments for your regular cancer care. These visits will be described in more detail later in this consent form. You may need to have a biopsy of your cancer. During this biopsy we will collect tissue for research purposes. There will be two visits to receive PDS0101 or PDS0101 plus pembrolizumab prior to your surgery or chemoradiotherapy. These two visits will last about 1.5-2 hours. You will also need to have an extra CT scan of your cancer prior to surgery. This CT scan will be paid for by the study. After that we would like to keep track of your health for up to 2 years.
Key Information	There are alternatives to taking part in this research. The research team will discuss the other treatment options with you. The main risks from this study are due to the study drugs being used. The most likely risks from the PDS0101 are pain and soreness at the injection site, headache, or nausea. The most common risks from pembrolizumab are itching of the skin, diarrhea (watery stools), and cough. The risks associated with study participation are completely described later in this form. Be sure to review them carefully. There are no additional costs to you for taking part in this study. The costs are described later in this consent form. Be sure to review them carefully. While our study is research and not guaranteed to offer help, you may benefit from the treatment if it works.
Learn More	If you are interested in learning more about this study, read the rest of this form carefully. The information in this form will help you decide if you want to participate in this research or not. A member of our research team will talk with you about taking part in this study before you sign this form. If you have questions at any time, please ask us.

Making Your Decision

Taking part in research is your decision. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep. A copy of this form will be put in your medical record.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

Contact Information

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigator(s):** David M. Routman, M.D. Kathryn M. Van Abel, M.D. Katharine A. Price, M.D. **Phone:** (507) 284-2511 **Institution Name and Address:** Mayo Clinic 200 First St SW Rochester, MN 55905
▪ Rights of a research participant	**Mayo Clinic Institutional Review Board (IRB)** **Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681
▪ Rights of a research participant ▪ Any research-related concern or complaint ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study	**Research Participant Advocate (RPA) (The RPA is independent of the Study Team) Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchparticipantadvocate@mayo.edu
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** (844) 217-9591

Other Information:
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.

A description of this research study will be available on http://www.clinicaltrials.mayo.edu. This website will not include information that can identify you. You can search this website at any time.

Why are you being asked to take part in this research study?

You are being asked to be in this study because you have been diagnosed with head and neck cancer that is considered to have a higher risk of returning, and you are planning to have surgery to remove the cancer plus radiation, or chemotherapy plus radiation to shrink the cancer.

The plan is to have about 24 patients take part in this study at Mayo Clinic.

Why is this research study being done?

In this study we want to find out more about how the PDS0101 vaccine with or without pembrolizumab may affect human papilloma virus (HPV)-related head and neck cancers.

Everyone in this study will receive PDS0101, which is "experimental." Experimental means that the FDA has not approved this vaccine for cancer treatment. However, the FDA has allowed the use of this vaccine in this research study.

Some patients will also receive pembrolizumab, an immune checkpoint inhibitor. Pembrolizumab is approved by the U.S. Food and Drug Administration (FDA) for the treatment of patients with melanoma, lung cancer, kidney cancer, colorectal cancer, and several other types of cancer. It is approved by the FDA for metastatic or recurrent head and neck cancers, and the FDA has allowed the use of this drug in this research study.

Information you should know

Who is Funding the Study?
PDS Biotechnology, Inc., will pay Mayo Clinic to cover costs related to running this study.

Information Regarding Conflict of Interest:
Your healthcare provider may be referring you to this research study. If your healthcare provider is also an investigator on this study, there is the chance that his or her responsibilities for the study could influence his or her recommendation for your participation. If you prefer, your healthcare provider will be happy to refer you to another investigator on the research study team for you to decide if you want to participate in the study and to see you for the research study activities while you are in the study.

How long will you be in this research study?

You will be in this study for up to 2 years.

You will receive treatment in this research study for about two months.

After you complete treatment in this research study, you may have surgery or chemoradiation, which are both standard of care, and you may have other treatments, such as radiation therapy and/or chemotherapy, as you and your doctor decide.

We will follow your health for up to two years. We may review your medical records, telephone you, or send you a request for information through the patient portal.

What will happen to you while you are in this research study?

You will receive two cycles of treatment on this study prior to your surgery or chemoradiation. Then you will have your surgery or chemoradiation and any other treatments your doctor has planned for your care. You will have one more visit for this study to make sure you are not still having any unwanted effects from this study. This visit will be at the same time you are starting your treatment with radiation and/or chemotherapy or when you are having your post-surgical check-up. We would like to see you again about 3-6 months after your surgery to see how you are doing. We will continue to keep track of your health for up to two years after you start this study.

Before starting this study
Before starting this study, you will participate in a screening period. The screening period will help the study doctor find out if you are eligible to enter the study. You will need to have the following exams, tests, or procedures as part of regular care for your cancer to find out if you can be in the study:

- Physical exam including complete medical history, height, weight, and vital signs
- ECOG performance status (measure of your ability to carry out daily activities)
- Routine blood tests
- Pregnancy test if you can become pregnant
- Consultation with a head and neck surgeon

- Imaging of your cancer
- Biopsy of your tumor, if deemed necessary by your treatment team

These exams, tests or procedures are part of regular clinical 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 decision will be up to the study doctor.

You will also have the following required tests which are part of the research study:

- Research blood tests (about 4 tablespoons)
- Research tissue samples (taken during the biopsy)

While you are on this study

Treatment on this study will be divided into two groups:
Group 1 will receive vaccination with PDS0101 on two occasions
Group 2 will also receive a dose of pembrolizumab prior to their two PDS0101 vaccines.

You and your doctor will know which group you will be assigned at the time of your appointment.

PDS0101 is given by injection into your arm. The PDS0101 dose is given as two injections under the skin at two separate visits. You will need to be monitored in the clinic for up to one hour after the first vaccine. If you do not have any strong reactions, you will only be monitored for 15 minutes after the second vaccine.

Pembrolizumab is given through a needle in a vein in your arm (IV) over about half an hour.

If you are receiving both PDS0101 and pembrolizumab, you will have the pembrolizumab first and wait for about half an hour before receiving the PDS0101.

You will also have an extra CT scan prior to surgery. This scan is done for research purposes, and you will not have to pay for it.

If you will not have surgery as part of your care, you will be offered a research biopsy to collect tissue for this study. You will not have to pay for this biopsy.

I agree to have a research biopsy as part of this study:

☐ Yes ☐ No Please initial here: _____Date: _____

Below is a chart to show you what will happen

Timing	What will happen
Pre-Study	• Routine physical exam • Routine blood tests • Routine measurement of your tumors by imaging • Biopsy of your cancer • Research blood collection (about 4 tablespoons)
Cycle 1, Day 1	**Group 1:** • Injection of PDS0101 into your upper arm • Monitoring of your vital signs for about one hour after PDS0101 **Group 2:** • Infusion of pembrolizumab over about 30 minutes • Monitoring of your condition for about 30 minutes after pembrolizumab • Injection of PDS0101 into your upper arm • Monitoring of your vital signs for about one hour after PDS0101
End of Cycle 1	• Routine physical exam • Routine blood tests • Review of your diary • Research blood draw (about 4 tablespoons)
Cycle 2, Day 1	**Group 1:** • Injection of PDS0101 into your upper arm • Monitoring of your vital signs for about 15 minutes if you did not have a reaction the first time. If you had a reaction the first time, your vital signs will be monitored for about one hour. **Group 2:** • Infusion of pembrolizumab over about 30 minutes • Monitoring of your condition for about 30 minutes after pembrolizumab • Injection of PDS0101 into your upper arm • Monitoring of your vital signs for about 15 minutes after PDS0101 if you did not have a reaction the first time. If you had a reaction the first time, your vital signs will be monitored for about one hour.
End of Cycle 2	• Routine physical exam • Routine blood tests • Review of your diary • Research blood collection (about 4 tablespoons) • Research CT scan

Timing	What will happen
Surgery or biopsy	• Research tissue collection - during your surgery to remove the cancer, some of the tissue removed will be saved for research. If surgery is not planned as part of your care, you may be offered a research biopsy.
At the time of your first post-surgery visit	• Routine physical exam • Routine blood tests • Research blood collection (about 4 tablespoons)
3-6 months after your surgery	• Routine physical exam • Routine blood tests

Post-visit patient tools:

- **Patient Vaccine Diary:** The study staff will provide you with instructions on how to complete a vaccine diary at vaccine administration visits (Cycles 1 and 2). You will be asked to record any reactions or side effects which you experience at the injection site for 7 days after it is given. Information collected on the diary includes any injection site reactions that occur, for example redness, warmth, swelling, pain, or tenderness, itching and skin discoloration or breakdown. Any medications for relief of injection site symptoms will also be recorded. If the reaction is severe or prolonged, you may be asked to take a picture and submit it to the study team.
- You will also receive an injection site reaction gauge. This is a diagram to help you measure your injection site reaction during the study.

Special Considerations

Because we need to understand how the human papilloma virus (HPV) affects the cancer and your body, we are requesting an additional item as a condition of participation in this pilot study.

As part of this study a portion of your blood will be sent to Naveris, Inc., to test for a biomarker of HPV-related cancers. The blood will not have your name or any information that Naveris can use to directly tie the sample to you. It will be sent with a code so we can link the results to you when they are returned.

If you choose to leave the study early or change your mind about giving permission to use your blood, you will not be able to withdraw any of your blood that was already collected or change the way the blood is used prior to leaving the study.

We will provide the results of this research testing to you or your doctor at the end of the study. You and your doctor can decide whether to put these results in your medical record.

What are the possible risks or discomforts from being in this research study?

Risks and side effects of PDS0101

Some patients may experience side effects that are typical of vaccines while in the study. Temporary pain or discomfort at the site of the vaccine injection is an example. Everyone taking part in the study will be watched for any side effects. Although extensive pre-clinical studies did not reveal any safety concerns, all individuals differ in their reactions to vaccines and the research may involve risks that are currently unknown. Although not predicted by studies with the vaccine in both animals and humans thus far, side effects are possible. The study staff may give you medicines to help lessen side effects if they are associated with significant discomfort. Most side effects are self-limiting and go away. Although very rare, in some cases, side effects to vaccines can be serious, long lasting, or may never go away.

The risks and side effects of the study PDS0101 vaccine are:

VERY COMMON (occurring in more than 10% of patients)

- Inflammation in the area of the injection, including redness, swelling, itching, pain, discomfort, warmth (injection site reaction)
- Pain or tenderness in the area of the injection
- Bruising in the area of the injection
- Bleeding at the injection site
- Skin discoloration in the area of the injection
- Headache
- Feeling tired or weak (fatigue)

COMMON (occurring in 5 to less than 10% of patients)

- Diarrhea – loose or watery stools
- Fever (pyrexia)

UNCOMMON (occurring in 1-<5% of patients) possible side effects are:

- Joint pain or swelling (arthralgia or arthritis)
- Hard or infrequent bowel movements (constipation)
- Cough, wheezing, trouble breathing, shortness of breath (dyspnea)
- Not feeling well, feeling “off” (malaise)
- Muscle soreness/pain including back pain, neck pain, jaw pain, non-cardiac chest pain or chest discomfort

- Sores, swelling, or pain in mouth, tongue, throat (stomatitis, oropharyngeal pain, laryngeal or pharyngeal inflammation) – may cause difficulty swallowing (dysphagia)
- Voice changes like hoarseness or rasp (dysphonia, laryngeal inflammation, laryngeal edema)
- Dry mouth
- Dizziness
- Low energy (lethargy)
- Weight loss or gain
- Pain or swelling in arms, hands, legs, or feet (edema)
- Trouble sleeping (insomnia)
- Fever or chills
- Low levels of thyroid hormone in the blood – may feel tired, cold, gain weight, have dry skin, low energy (hypothyroidism)
- Influenza-like illness – may have body aches, fever, chills, cough, congestion
- Indigestion (sour stomach), nausea or vomiting – discomfort, belly pain, burning, heartburn, belching, bloating, feeling sick to your stomach, throwing up (dyspepsia)
- Heart rhythm changes such as rapid heartbeat (tachycardia) or slowed heart rate (bradycardia)
- Increased blood pressure (hypertension)
- Hardening or lump (induration) or mass under the skin especially in the area of the injection
- Rash (dermatitis) – including redness (discoloration, erythema), bumps (acneiform, maculopapular), hives (urticaria), itching, swelling
- Change in lab values as seen on blood or urine tests – may have no symptoms or vague symptoms (including but not limited to any of the following: lymphopenia, thrombocytopenia, proteinuria, glycosuria, hemoglobinuria, nitrituria, hypophosphatemia, hyperphosphatemia, hyperkalemia, hyponatremia, liver function tests, kidney function tests) – your doctor will tell you if any lab changes found need follow-up
- Emotional distress or anxiety (feeling nervous or fearful)
- Confusion, disorientation, impaired consciousness, difficulty with concentration or memory – may develop rapidly
- Pain – including tenderness, soreness, or discomfort

Although rare and not anticipated, hypersensitive reactions may be mild (such as rash and fever) or may range to severe (such as anaphylaxis). Symptoms of a severe allergic reaction may include difficulty breathing and/or swallowing, wheezing, hives, swelling of the face, eyes, lips, or tongue, or low blood pressure leading to shock.

In studies of PDS0101 to date, no severe reactions or deaths have been seen associated with vaccination. As with any new product, the possibility of these risks should be considered.

After your first vaccine dose, you must remain in the study doctor's office for the first hour so the study staff can take your vital signs (temperature, blood pressure, heart and respiratory rate) and monitor you for possible immediate vaccine reactions and side effects. If you do not have any significant immediate reactions following your first vaccine, you will only have to remain in the doctor's office for 15 minutes after your second vaccine dose (Cycle 2).

If you receive the combination of PDS0101 and pembrolizumab you may see the same side effects listed above as well as those listed below.

UNCOMMON (occurring in 1% to <5% of patients)
Out of 100 people who receive PDS0101 and pembrolizumab, at least 1 but less than 5 people may have the following:

- Anemia – low level of red blood cells – may feel tired, weak
- Adrenal insufficiency – may feel tired or weak, have weight loss, low blood pressure, salt craving or skin changes
- Acute kidney injury including kidney failure
- Change in lab values as seen on blood or urine tests – may have no symptoms or vague symptoms (including but not limited to any of the following: hypocalcemia, lipase increase, liver function tests [such as hyperbilirubinemia, elevated transaminases], kidney function tests) – your doctor will tell you if any lab changes found need follow-up
- Buildup of fluid around the heart (pericardial effusion) – may cause shortness of breath, chest pain
- Colitis – the large intestine (colon) becomes inflamed – may cause belly pain, ulcers, bloating, diarrhea, blood in stool
- Eye problems including pink eye (conjunctivitis), dry eye, trouble seeing (visual impairment)
- Encephalitis -Inflammation of the brain or spinal cord with confusion and fever - may also include disorientation, memory problems, seizures (fits), changes in personality and behavior, difficulty speaking, weakness or loss of movement in some parts of your body, and loss of consciousness
- Loss of appetite – not feeling hungry, not wanting to eat
- Gastritis – inflammation of the stomach lining- may have pain, nausea, vomiting
- Hyperglycemia – increase in blood sugar level – may need to take or increase medicines to control blood sugar
- Hyperthyroidism – also called "overactive thyroid" - may have weight loss, hand tremors, rapid or irregular heartbeat

- Infusion related reaction, where you may feel dizzy or faint, feel flushed, get a rash, have a fever, feel short of breath, experience a decrease in your blood pressure at the time of receiving your infusion (IV) or just after, or have pain at the site of infusion
- Mucosal inflammation – may affect any part of the mouth, nose, throat, stomach (gastrointestinal system), anus, urinary tract, vagina
- Muscle spasms – Charley horse, twitching, cramping, pain
- Nerve problems – numbness, tingling, loss of sensation (hypoesthesia, peripheral neuropathy)
- Orthostatic hypotension – a form of low blood pressure that happens on rising from a sitting or lying down position – may feel dizzy, lightheaded or faint
- Pneumonitis – inflammation of the lungs that may cause difficulty breathing, coughing, wheezing, shortness of breath (dyspnea)
- Skin problems – rash or irritation such as dry skin, redness, blistering, itching, oozing, peeling, crusting, including perioral dermatitis, general dermatitis
- Trouble urinating – peeing too much or too often (polyuria, pollakiuria)

Risks and side effects of pembrolizumab (MK-3475)
Please note in this study you will only receive two doses of pembrolizumab, so the study doctors believe these effects are less likely to happen in this study.

Pembrolizumab works by helping your immune system to fight your cancer. However, pembrolizumab can also cause your immune system to attack normal organs and tissues in your body and can affect the way they work, which can result in side effects. These side effects may be serious (i.e., causing hospitalization) or be life-threatening, may result in death, and/or may occur after you stop taking pembrolizumab. These side effects can affect more than one of your normal organs and tissues at the same time.

VERY COMMON
Out of 100 people who receive pembrolizumab, 20 or more people may have the following:

- Itching of the skin
- Loose or watery stools
- Cough

COMMON
Out of 100 people who receive pembrolizumab, at least 5 but less than 20 people may have the following:

- Joint pain
- Rash
- Fever
- Back pain

- Pain in your belly
- Loss of skin color
- Not enough thyroid hormone, so you may feel tired, gain weight, feel cold, or have infrequent or hard stools (hypothyroidism)
- Low levels of salt in the blood that may cause you to feel tired, feel confused, have a headache, and/or feel sick to your stomach (hyponatremia)

UNCOMMON
Out of 100 people who receive pembrolizumab, at least 1 but less than 5 people may have the following:

- Inflammation of the lungs, so you may feel short of breath and cough (pneumonitis)
- Too much thyroid hormone, so you may feel anxious, feel angry, have trouble sleeping, feel weak, tremble, sweat, feel tired, have loose and watery stools (hyperthyroidism)
- Infusion reaction, where you may feel dizzy or faint, feel flushed, get a rash, have a fever, feel short of breath, experience a decrease in your blood pressure at the time of receiving your infusion (IV) or just after, or have pain at the site of infusion
- Inflammation of the bowels/gut, which may cause severe pain in your belly with loose or watery stools, and black, tarry, sticky stools or stools with blood or mucus (colitis)
- Inflammation of the skin so you may have peeling of the skin, itchiness, and/or skin redness. The skin inflammation (i.e., peeling, itching and redness) could also be widespread throughout your body. More severe skin reactions may involve the inside of your mouth, the surface of your eye and genital areas, and/or may cause the top layer of your skin to peel from all over your body which can cause severe skin reactions, including Stevens-Johnson syndrome or toxic epidermal necrolysis [TENS])

RARE
Out of 100 people who receive pembrolizumab, less than 1 person may have the following:

- Inflammation of the nerves that may cause pain, weakness, or tingling in your hands and feet, and may spread to your legs, arms, and upper body, leading to severe muscle weakness and possible temporary paralysis (Guillain-Barré syndrome)
- Inflammation of the muscles, so you may feel weak or have pain in your muscles (myositis)
- Inflammation of the pancreas (a gland in your abdomen that controls sugar levels), so you may have severe pain in the top part of your belly that may move to your back, feel sick to your stomach, and have vomiting that gets worse when you eat (pancreatitis)
- Inflammation of the eye, so you may have eye redness, blurred vision, sensitivity to light, eye pain, see floaters, or have headaches (uveitis)
- Inflammation of the liver that may make you feel sick to your stomach and vomit, feel like not eating, feel tired, have a mild fever, a pain in the right side of your belly, yellow eyes and skin, and dark urine (hepatitis)

- Inflammation of the pituitary gland (a gland in the head), which may cause you to feel sick to your stomach or have headaches, changes in your behavior, double vision, few to no menstrual cycles, weakness, vomiting and dizziness, or fainting (hypophysitis)
- Adrenal glands (glands on top of the kidneys) that may not make enough hormone, which could cause tiredness, weight loss, muscle weakness, feeling faint, having joint, muscle, and bellyaches, nausea, vomiting, loose or watery stools, fever, salt craving, and sometimes darkening of the skin like a suntan (adrenal insufficiency)
- Type 1 diabetes, a condition that can cause too much sugar in your blood, feeling thirstier than usual, frequent urination, and weight loss. You are likely to need regular insulin shots
- Inflammation of the kidney, so you may pass less urine or have cloudy or bloody urine, swelling, and low back pain (nephritis)
- Inflammation of the middle layer of your heart wall that may cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain, shortness of breath, and swelling of the legs. You may experience a fast or irregular heartbeat that may cause dizziness or fainting (myocarditis)
- Inflammation of the thyroid gland, an organ that makes and stores thyroid hormones. This condition may lead to change in your heartrate, blood pressure, body temperature, and the rate at which food is converted into energy (thyroiditis)
- A condition that may make you feel weak and tired and may cause drooping of the eyelids, blurred or double vision, difficulty swallowing, slurred speech, weakness in your arms and legs, or difficulty breathing (myasthenic syndrome/myasthenia gravis including exacerbation)
- The formation of small clusters of immune cells (called granulomas) in parts of your body such as your lymph nodes, eyes, skin, or lungs (sarcoidosis)
- Inflammation of the brain with confusion and fever - may also include disorientation, memory problems, seizures (fits), changes in personality and behavior, difficulty speaking, weakness or loss of movement in some parts of your body, and loss of consciousness (encephalitis)
- Inflammation of the spinal cord with pain, numbness, tingling, or weakness in the arms or legs, bladder or bowel problems including needing to urinate more frequently, urinary incontinence, difficulty urinating, and constipation (myelitis)
- Inflammation of the blood vessels (vasculitis). Symptoms will depend on the particular blood vessels that are involved in the inflammatory process, for example, if it is your skin, you may get a rash. If your nerves are not getting enough blood, you could have numbness and weakness. You may also experience fever, weight loss, and fatigue.

Additionally, since pembrolizumab was approved in September 2014, the following side effects have been reported by people receiving pembrolizumab. These side effects were voluntarily reported from a group of people of unknown size. It is not possible to estimate the frequency of this side effect:

- Inflammation of the joints which may include joint pain, stiffness and/or swelling (arthritis)
- Severe responses of the immune system that cause the body to attack its own blood cells, spleen, liver, lymph nodes, skin, and brain. This reaction may include fever, rash, inflammation of the liver, yellowing of the skin, an enlarged liver and spleen, low blood counts, and enlarged lymph nodes. The nervous system may also be affected and cause confusion, seizures, and even coma (hemophagocytic lymphohistiocytosis (HLH))
- Vogt-Koyanagi-Harada (VKH) Syndrome – an immune response of skin cells (melanocytes) which affects eyes, ears, nervous system, and skin; damage from VKH may be permanent
- Inflammation and scarring of the bile ducts (tubes that carry digestive fluid that is made in the liver). This can cause symptoms similar to those seen with inflammation of the liver (hepatitis) such as pain in right side of your belly, yellow eyes and skin, feeling tired, and itching (sclerosing cholangitis).

We do not know all the side effects that may occur with pembrolizumab. The side effects of pembrolizumab may cause delays to your treatment with radiation and may also delay your surgery.

Other Risks

Blood draws

The risks of drawing blood include pain, bruising, lightheadedness, and/or fainting, or rarely, infection at the site of the needle stick.

Pregnancy and Birth Control:

It is not known if the study drugs may affect an unborn or nursing baby or if the study drugs can affect sperm. If you are pregnant, trying to become pregnant or breast-feeding, you may not be in the study. The study doctor will perform a pregnancy test before the start of and during the study if you are able to have a baby.

For Persons Able to Become Pregnant

If you are sexually active and able to become pregnant, you must agree to use contraception during intercourse with any person able to father a child. Discuss which methods are appropriate with your doctor.

You must use birth control for the entire study and for at least 120 days after your last dose of pembrolizumab or PDS0101.

If you miss a period, or think you might be pregnant during the study, you must tell the Principal Investigator immediately. The Principal Investigator may ask for your permission to collect information about the outcome of your pregnancy and your newborn.

For Persons Able to Father a Child
If you are sexually active, and able to father a child, you must agree to use **contraception** during intercourse with any person able to become pregnant. Discuss which methods are appropriate with your doctor.

You must use birth control for the entire study and for at least 120 days after your last dose of pembrolizumab or PDS0101.

If your female partner thinks they might have become pregnant while you are in the study or for 30 days after your last dose of pembrolizumab or PDS0101, you must tell your study doctor immediately. The study doctor may ask for your partner's permission to collect information about the outcome of the pregnancy and the newborn. You won't have to stop taking the study drug or stop taking part in the study if your partner becomes pregnant.

Biopsies
Biopsies are normally performed under the guidance of an imaging technique such as CT or ultrasound. Each procedure requires a separate consent prior to the biopsy. If you are able to become pregnant, you must have a pregnancy test prior to the biopsy.

The risks of biopsies may include:

- Pain and discomfort - the amount of pain and discomfort will vary, depending on the location of the biopsy site
- Minor bleeding at the biopsy site
- Tenderness at the biopsy site
- Scarring at the biopsy site
- Rarely, an infection at the biopsy site

Uncommonly, complications from biopsies can be life threatening. As with any interventional procedure, other complications from bleeding or organ damage may occur. These complications might require surgery to fix them.

Radiation Risk
You will be exposed to radiation if CT is used to perform the biopsy and from the additional CT scan prior to surgery. The amount of radiation has a low risk of harmful effects.

If you are able to become pregnant, you must have a pregnancy test prior to the biopsy.

Genetic Information Nondiscrimination Act (GINA)
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 when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans must follow this law.

Be aware that this new Federal law doesn't protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Risks Associated with Genomic Testing
This study involves testing your DNA, which is the genetic information you inherited from your parents (also known as genetic testing). This testing may include whole genome sequencing (mapping your entire genetic code). You will not be notified of the genetic test results and they will not be put into your medical record.

Despite the GINA protections and the best efforts of the research team, there may still be a risk if information about you were to become known to people outside of this study.

Genetic information is unique to you, even without your name or other identifiers. For this reason, genetic information like DNA may be used to identify you and possibly your family members. We have procedures (such as, labeling your biospecimens with a password protected code known only to select research staff) to prevent people working with your DNA from discovering if it belongs to you. However, there is the risk this can happen as new ways of tracing genetic information are being developed that may make re-identification of genetic information possible.

Standard of Care Risks
Your doctor will discuss the risks of these tests and procedures, which are part of regular care for your cancer:

- Surgery to remove your cancer
- Imaging of your cancer (CT, MRI, etc.)
- Additional therapy for your cancer including radiation therapy and chemotherapy

Confidentiality Risk
As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk.

Unforeseeable Risks
Many side effects go away shortly after the treatment is stopped, but in some cases side effects can be serious, long lasting, or may never go away. There may be a risk of death. Some side effects may not be known. Side effects may range from mild to life-threatening. Other drugs may be given to make side effects less serious and less uncomfortable. Talk to the researcher and/or your healthcare provider about side effects and ask any other questions.

Are there reasons you might leave this research study early?

Taking part in this research study is voluntary. You may decide to stop at any time. You should tell the researcher if you decide to stop, and you will be advised whether any additional tests may need to be done for your safety.

In addition, the researchers or Mayo Clinic may stop you from taking part in this study at any time:

- If it is in your best clinical interest,
- If you do not follow the study procedures,
- If the study is stopped.

If you leave this research study early, or are withdrawn from the study, no more information about you will be collected; however, information already collected about you in the study may continue to be used.

We will tell you about any new information that may affect your willingness to stay in the research study.

What if you are injured from your participation in this research study?

Where to get help:

If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries:

PDS Biotechnology will offer to pay for medical treatment of research-related injuries directly resulting from the proper application of the study drug. The Sponsor may decide not to pay for several reasons. The Sponsor may not pay if the Sponsor concludes the injury happened because you did not follow the study directions, or the injury resulted from your actions. The Sponsor may not consider the worsening of an existing health condition to be a research-related injury. In the case of injury resulting from your participation in this study, you do not lose any of your legal rights to seek payment by signing this form. Contact the Principal Investigator, who can help you obtain this reimbursement.

If PDS Biotechnology pays for research-related injury costs and you are eligible for Medicare, federal law requires PDS Biotechnology to inform the Centers for Medicare & Medicaid Services (the agency responsible for the Medicare program). Information, such as your name, date of birth, sex, and Medicare ID number (if you have one), may need to be shared with PDS Biotechnology and the Centers for Medicare & Medicaid Services.

What are the possible benefits from being in this research study?

This study may not make your health better. However, it may help other cancer patients in the future.

What alternative do you have if you choose not to participate in this research study?

You don't have to be in this study to receive treatment for your condition. Your other choices may include:

- Treatment for your cancer without being on a study
- Treatment on a different research study
- No treatment

Talk to the Principal Investigator or your doctor if you have any questions about any of these choices.

What tests or procedures will you need to pay for if you take part in this research study?

You will not need to pay for tests and procedures which are done just for this research study. These tests and procedures are:

- Study drugs PDS0101 and pembrolizumab and their administration
- One head and neck CT scan just prior to surgery (after the vaccines are completed)
- Research biopsy if one is needed
- Research testing on your blood and tumor tissue

However, you and/or your health plan will need to pay for all other tests and procedures that you would normally have as part of your regular medical care. These tests and procedures include:

- Biopsy of your cancer, if needed for your care
- Tumor resection (surgery to remove your cancer), if done
- Treatment for your cancer with chemotherapy and/or radiation
- Routine blood testing
- Exams and consults
- Pregnancy tests (if applicable)
- Imaging of your cancer (for example with CT, PET-CT, MRI)

Before you take part in this study, you should call your insurer to find out if the cost of these tests and/or procedures will be covered. Some insurers will not pay for these costs. You will have to pay for any costs not covered by your insurance, Including copayments and deductibles.

If you have billing or insurance questions call Patient Account Services at the telephone number provided in the Contact Information section of this form.

Will you be paid for taking part in this research study?

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

There is a very small chance that some commercial value may result from the use of your donated samples. This result could include new products like a drug or a test to diagnose a disease. If that happens, you won't be offered a share in any profits.

Will your information or samples be used for future research?

Submission of blood and tissue samples is required to take part in this study. These samples will be collected prior to starting the study, and at the time of surgery to remove the cancer, and one sample after your surgery, before you start radiation and/or chemotherapy.

Some of your blood samples will be sent to Naveris, Inc. for required research testing as part of this study. The samples will be coded so no one at Naveris will know the samples are yours. Naveris will test the samples and return the results to the principal investigator for this study. Naveris will not keep the samples for future unspecified research.

Your information and samples will be kept by Mayo Clinic. Mayo Clinic can use your data and samples for research purposes only as described in the research study. Your data and samples will be kept by Mayo Clinic in a coded format, which protects your identity. Mayo Clinic may destroy the samples at any time without telling you. We will test your tissue and blood as part of this study.

In addition, we would like to keep your sample for future research that is not planned as part of this study. You can still take part in this current study even if you don’t want your sample used for future research. If you agree to give your sample, it will be the property of Mayo Clinic.

Researchers at Mayo Clinic who aren't involved with this study may ask to use your sample for future research. Researchers at other institutions may also ask for a part of your sample for future studies. Your sample will be sent to researchers in a coded format, which protects your identity.

Some future studies may examine your DNA, which is the genetic information you inherited from your parents (genetic testing). The study doctor may contact you if there are findings which may be useful for your health care. You would be given general information on the potential risks, benefits, and costs of choosing to learn about the findings.

To support future research, de-identified genetic information may be placed in databases accessible by the internet. Some of the information may be available to anyone using the internet, and some will be released only to approved researchers. Combined study information (including genomic summary results) may be published, but the information will not identify you.

Even though information traditionally used to identify you will not be shared, people may develop ways in the future to allow someone to link your genetic information back to you. For this reason, confidentiality cannot be guaranteed. It is also possible that re-identified information could be used in discriminating ways, and there could be additional unknown risks. We will make every effort to protect your confidentiality.

Please read the following four statements and mark your choices:

I permit my sample to be stored and used in future research on cancer at Mayo Clinic:

☐ Yes ☐ No Please initial here: _____Date: _____

I permit my sample to be stored and used in future research at Mayo Clinic to learn about, prevent, or treat any other health problems:

☐ Yes ☐ No Please initial here: _____Date: _____

I permit Mayo Clinic to give my sample to researchers at other institutions:

☐ Yes ☐ No Please initial here: _____Date: _____

I agree to have my coded genetic information and coded medical information placed in password-protected secured databases for research analyses.

☐ Yes ☐ No Please initial here: _____Date: _____

You may withdraw your consent for future use of your information and/or samples at any time, by writing to the Principal Investigator at the address provided in the "Contact Information" section of this consent form.

Your information and/or samples would be removed from any repository where they are stored, if possible. Information and/or samples already distributed for research use will not be retrieved. Because we cannot predict how your sample will be used in the future, we cannot promise that samples can be retrieved and destroyed.

It is possible that information identifying your samples or your data could be removed. These samples and data will no longer be linked to you. If that were to happen, the samples and data could be used for future research studies or given to another researcher without asking for your permission.

How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study.

All of your research samples given to Mayo Clinic will be labeled with a code number and kept in locked storage. Only your study team will be able to link your samples with your identity. No one working with your samples will know your identity. If the results of the research are made public, information that identifies you will not be used.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

Your health information may be collected from:

- Past, present, and future medical records.
- Research procedures, including research office visits, tests, interviews, and questionnaires.

Your health information will be used and/or given to others to:

- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:

- Mayo Clinic research staff involved in this study.
- Other Mayo Clinic staff involved in your clinical care
- Mayo Clinic, as the sponsor of this study and the people or groups hired by the sponsor to help perform this research.
- PDS Biotechnology Inc, the company that is providing the study drug, PDS0101
- The Mayo Clinic Institutional Review Board that oversees the research.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.
- A group that oversees the data (study information) and safety of this research.

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you but does not include information that directly identifies you. This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media), information that identifies you will not be used.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, or copy (using paper, digital, photographic, or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private, and it may no longer be protected by the Privacy Rule.

Your Rights and Permissions

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study. Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with Mayo Clinic.

If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
Plummer Building PL 3-02
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: researchparticipantadvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts forever, unless you cancel it.

Enrollment and Permission Signatures

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

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature