Washington University in St. Louis

INFORMED CONSENT DOCUMENT

Project Title: A Phase II Trial of ADI-PEG 20 in Combination with Gemcitabine and Docetaxel for the Treatment of Soft Tissue Sarcoma, Osteosarcoma, Ewing's Sarcoma, and Small Cell Lung Cancer

Principal Investigator: Brian Van Tine, M.D., Ph.D.

Research Team Contact: Brian Van Tine, M.D., Ph.D. – (314) 362-7997

- If you are the parent/guardian of a child under the age of 18 who is being invited to participate in this study, the word "you" in this document refers to your child. As the parent/guardian, you will be asked to read and sign this document to give permission for your child to participate.
- If you are under the age of 18 and reading this document, the word "you" in this document refers to you. You will be asked to read and sign this document to indicate your willingness to participate.

This consent form describes the research study and helps you decide if you want to participate. It provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights and responsibilities as a research participant. By signing this form, you are agreeing to participate in this study.

- You should read and understand the information in this document including the procedures, risks and potential benefits.
- If you have questions about anything in this form, you should ask the research team for more information before you agree to participate.
- You may also wish to talk to your family or friends about your participation in this study.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

KEY INFORMATION

This is a research study conducted by Dr. Brian Van Tine having to do with adding the investigational drug ADI-PEG 20 to standard chemotherapy given to treat of soft tissue sarcoma. You are invited to be in this study because you have been diagnosed with a soft tissue sarcoma that cannot be removed surgically or has spread to other parts of your body or you have been diagnosed with osteosarcoma, Ewing's sarcoma, or small cell lung cancer that cannot be removed surgically and would be treated with gemcitabine with or without docetaxel as part of your routine care. You should carefully consider the information in this consent document and discuss it with the research team. You should understand why you might want to participate, or why you might not want to participate. It is your choice whether to participate or not.

If you agree and sign this consent, you will be volunteering to participate in the research study. The research team must give you a copy of this signed consent document.

1. **What is this study about?**
   This study is being done to learn more about adding the investigational drug ADI-PEG 20 to a standard treatment regimen called gem-tax (the chemotherapy drugs gemcitabine and docetaxel). Gem-tax is a treatment regimen that people with your disease receive to treat their cancer.

2. **Why should I consider participating?**
   The researchers are looking at how the addition of ADI-PEG 20 affects your tumor's response to treatment and whether it impacts the side effects you experience. Participating in this study will help researchers learn more about using ADI-PEG 20 as a treatment for soft tissue sarcoma, osteosarcoma, Ewing's sarcoma, and small cell lung cancer.

3. **What will I be asked to do?**
   This study includes some procedures you might have for your care if you weren't in this study. We will ask you to come in once a week for treatment. On the first day of treatment (Day -7), you will receive ADI-PEG 20 (as an injection into your shoulder or buttock). On Day 1 of each cycle, you will receive gemcitabine IV (through a vein) and ADI-PEG 20. On Day 8 of each cycle, you will receive gemcitabine, docetaxel IV, and ADI-PEG 20. On Day 15 of each cycle, you will receive ADI-PEG 20. You will have blood drawn for research purposes on Day -7, Day -1 (the day before your first dose of gemcitabine), Day 1 of each cycle, and Day 8 of each cycle. You may also have a tumor biopsy on Day -7 (or up to 2 weeks before that) and Day -1 (or the day before or after). Your visits may take several hours depending on the procedures you are having at each visit. You will be in the study for as long as you are benefitting from treatment.

   You may choose to stop participating and withdraw from the study at any time. If you withdraw from the study, the research team may continue to use the information already collected about you.

4. **What are the risks?**
   There are some risks to you if you agree to volunteer for this study. The most serious/most common risks are fatigue, nausea, vomiting, hair loss, infection, bruising, bleeding, anemia, numbness and tingling, swelling, sores in the mouth, and pain. The risks to you are described in more detail later in this consent document.

5. **What are the benefits to me? To others?**
   There may be no direct benefit to you. However, we hope that, in the future, other people might benefit from this study because it will help researchers learn more about using ADI-PEG 20 as part of the treatment for soft tissue sarcoma, osteosarcoma, Ewing's sarcoma, and small cell lung cancer.

6. **Is there any financial cost to me?**
   As part of this study you will receive tests and procedures that are similar to what you would receive during routine clinical care of your condition. Your health plan/insurance company will be billed for some or all of these costs, and you will be responsible for any co-pays and deductibles that are normally required by your health plan/insurance. Polaris Pharmaceuticals is providing the ADI-PEG 20 at no cost to you.

7. Will my information be confidential?
Yes, your identity will be kept confidential. Your information will be available only to those who are working on this study.

8. Who is the sponsor?
Polaris Pharmaceuticals is providing the ADI-PEG 20 for this research study. The National Institute of Health (NIH) is also funding this research study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We invite you to participate in this research study because you have been diagnosed with a soft tissue sarcoma that cannot be removed surgically or has spread to other parts of your body or you have been diagnosed with osteosarcoma, Ewing's sarcoma, or small cell lung cancer that cannot be removed surgically and would be treated with gemcitabine with or without docetaxel as part of your routine care..

The purpose of this research study is to learn more about adding the drug ADI-PEG 20 to a standard treatment regimen called gem-tax (the chemotherapy drugs gemcitabine and docetaxel) and how the addition of ADI-PEG 20 affects your tumor's response to treatment and the side effects you experience.

ADI-PEG 20 is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration.

Gemcitabine is approved by the U.S. Food and Drug Administration to treat ovarian cancer, breast cancer, non-small cell lung cancer, and pancreatic cancer. However, the use of gemcitabine is considered investigational in this study.

Docetaxel is approved by the U.S. Food and Drug Administration to treat breast cancer, non-small cell lung cancer, prostate cancer, gastric (stomach) cancer, and head and neck cancer. However, the use of docetaxel is considered investigational in this study.

WHAT WILL HAPPEN DURING THIS STUDY?

All treatment will be given in either the outpatient or inpatient setting at Siteman Cancer Center. We feel it is important to remind you that any procedures regardless of whether they are tests you would have if you did not take part in the research or are research-related will require you to remain at the Siteman Cancer Center up to several hours to complete the necessary testing. It is important that you are able to be available to complete the procedures at each visit to ensure that your safety and treatment needs are met.

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

- Physical exam, including taking of vital signs, reviewing your medical history, and talking about any symptoms or health problems you're having

- Blood tests to check your blood counts and organ function (approximately 2 teaspoons of blood will be drawn)
- A pregnancy test if you are a woman of childbearing potential (approximately 1 teaspoon of blood will be drawn, if necessary)
- Electrocardiogram (ECG) to check the function of your heart. You will be asked to lie flat on a table and several small electrode pads (like stickers) are stuck on your arms, legs, and chest. The electrodes are connected to a machine that records the electrical signals of each heartbeat and monitors how your heart is working.
- CT scan (computerized tomography, which uses x-rays to create a picture of the bones and soft tissues in your body) to check on the status of your disease. In some cases, a contrast medium will be used and you must not eat or drink anything for 4 hours before the test (the doctor will tell you if this is the case). A "contrast medium" is a liquid or solid that helps make a sharper image from the scan. Before the scan, you will need to remove all jewelry. During the scan, you will lie on your back on an X-ray table. A strap may be placed across your body to prevent movement so that the X-ray will be clear. The table will then slide into a large tunnel-shaped machine.

It is possible that after your medical history and the results from the above tests and procedures are reviewed, you will not be able to continue in this study. If this occurs, your study doctor will go over the reasons with you.

Procedures throughout the study:
If you continue in this study, you will begin receiving treatment. Treatment is the same for everyone regardless of whether you have a soft tissue sarcoma, osteosarcoma, Ewing's sarcoma, or small cell lung cancer.

Gemcitabine is given intravenously (through a vein) over the course of about 90 minutes on Days 1 and 8 of each 21-day cycle. Docetaxel is given intravenously over the course of about 60 minutes on Day 8 of each cycle. ADI-PEG 20 is given as an intramuscular injection (either into a shoulder or a buttock) a week before you begin treatment with gem-tax and again on Days 1, 8, and 15 of each cycle.

While you are receiving treatment on this study, you will have the following tests and procedures:

- Physical exam, including taking of vital signs and talking about symptoms or health problems you're having on Day 1 of each cycle
- Blood tests to check your blood counts on Day 1 and Day 8 of each cycle; if you are taking a blood thinning medication, you will also have blood tests to check your blood counts on Day 15 of each cycle (approximately 1 teaspoon of blood will be drawn at each time point)
- Blood tests to check your organ function on Day 1 of each cycle (approximately 1 teaspoon of blood will be drawn at each time point)
- CT scan approximately every 6 weeks
- Blood draw for research purposes (approximately 2 teaspoons) at the following time points:
  - One week before gem-tax treatment starts (prior to ADI-PEG 20)
  - One day before gem-tax treatment starts
  - Day 1 of each cycle

- Day 8 of each cycle

Additionally, if you have small cell lung cancer, you will have a tumor biopsy for research purposes at the following time points:

- One to 3 weeks before gem-tax treatment starts (prior to ADI-PEG)
- One day before gem-tax treatment starts (may be done 2 days before or on the day you start receiving gemcitabine)

A small amount of archival tissue (tissue from a previous surgery or biopsy) will also be requested for all patients for research purposes.

You may continue to receive treatment for as long as you are benefiting, or until you or your doctor decide to stop your treatment. After your 8th cycle of gem-tax, you may discontinue those drugs and continue receiving ADI-PEG 20 by itself if your doctor feels it's in your best interests.

After you finish treatment, you will be monitored for 30 days to look at any side effects you might be experiencing. If you come off of treatment for any reason other than progressive disease, you will have a CT scan every 6 to 12 weeks for 5 years or until disease progression or initiation of new treatment. Your medical record will be accessed after you come off study to look up your health status and the status of your disease at 5 years after the end of treatment.

Will you save my samples or research data to use in future research studies?

As part of this study, we are obtaining tissue, blood, and data from you. We would like to use this tissue, blood, and data for studies going on right now as well as studies that are conducted in the future. Your tissue, blood, and data may also be used for broad sharing throughout the research community. This means your tissue, blood, and data may be used for any sort of research and not just research related to your current condition, including research to develop investigational tests, treatments, drugs or devices that are not yet approved by the U.S. Food and Drug Administration. These researchers may be at Washington University, at other research centers and institutions, or commercial sponsors of research. It is unlikely that what we learn from these studies will have a direct benefit to you. There are no plans to provide financial compensation to you should this occur. By allowing us to use your tissue, blood, and data you give up any property rights you may have in the tissue, blood, and data.

One way in which we may share your data with others is by putting it into a large database of information, called a data repository. If your data is placed in one of these repositories it will be placed in the "controlled-access" portion of the repository. This means that only qualified researchers, who have received permission from individuals that monitor the access to and use of the data, will be able to look at and use your information. Before we put it in this repository, we will remove any information, such as your name and birthdate, that might easily identify you. Even though these data will not have your name or other identifying information associated with it, it is still possible that someone may be able to trace these data back to you because genetic information is unique. Although your individual data will only be in the controlled access database certain summary information may be available to the general public.

This future research may include genetic research. Genes are a unique combination of molecules (called

DNA) that we inherit from our parents. There are millions of tiny differences in our genes that determine things like our height or the color of our eyes. Some of these differences may make some people more or less likely to develop certain diseases or conditions or to have certain characteristics. The future genetic research may include looking at the difference in genes between different groups of people or it may include studying your entire DNA sequence. Studying your entire DNA sequence will provide a detailed description of your DNA and is sometimes called whole genome sequencing.

If you change your mind and do not want us to store and use your tissue, blood, and data for future research you should contact the research team member identified at the top of this document. The tissue, blood, and data will no longer be used for research purposes. However, if some research with your tissue, blood, and data has already been completed, the information from that research may still be used. Also, if the tissue, blood, and data has been shared with other researchers it might not be possible to withdraw the tissue, blood, and data to the extent it has been shared.

Please place your initials in the blank next to Yes or No for each of the questions below:

My tissue, blood, and data may be stored and used for future research as described above.

_____ Yes **_____ No**
Initials **Initials**

My tissue, blood, and data may be shared with other researchers and used by these researchers for the future research as described above.

_____ Yes **_____ No**
Initials **Initials**

Identifiers may be removed from your private information, including blood, tissue, and data and used for future research or shared with others. If this occurs, we will not ask you for additional consent.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 70 people will take part in this study conducted by investigators at this site. An additional 20 people will be enrolled at other institutions across the country for a total of approximately 90 people.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for as long as you are benefitting from treatment, or until you or your physician believes it is no longer in your best interests to continue in the study. You will be followed to check on your health and wellbeing for 5 years after you stop study treatment.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.
Some risks described in this consent document, if severe, may cause death.

Risks of ADI-PEG 20

Common

- Fatigue

Less common

- Pain, redness, itching, and swelling at the injection site
- Fever
- Rash
- Itching
- Nausea
- Vomiting
- Diarrhea
- Excess uric acid in the bloodstream (gout)
- Loss of appetite
- Low white blood cell count, which can increase your risk of infection
- Low platelet count, which can increase your risk of bleeding
- Low red blood cell count (anemia), which can cause fatigue
- Elevated liver enzymes, which can indicate liver damage

Rare but serious

- Anaphylaxis (a serious, potentially life-threatening allergic reaction); symptoms include itching, throat or tongue swelling, shortness of breath, vomiting, lightheadedness, and low blood pressure
- Serum sickness (a reaction that is similar to an allergy to the medication); symptoms include fever, rash, and joint pain or swelling
- Seizures
- Sepsis

Risks of Gemcitabine

Likely

- Flu-like symptoms of muscle pain, fever, headache, chills and fatigue
- Nausea, vomiting
- Rash
- Hair loss
- Infection, especially when white blood cell count is low
- Bruising, bleeding
- Anemia which may require a blood transfusion
- Muscle weakness
- Blood in urine
- Feeling of "pins and needles" in arms and legs
- Numbness and tingling of the arms and legs
- Tiredness
- Difficulty sleeping

- Swelling of arms, legs

Less Likely

- Swelling and redness of the area of radiation
- Blisters on the skin
- Diarrhea, constipation
- Sores in mouth which may cause difficulty swallowing
- Liver damage which may cause yellowing of eyes and skin, swelling
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Scarring of the lungs
- Shortness of breath
- Fluid in the organs which may cause low blood pressure, shortness of breath, swelling of ankles

Rare and Serious

- Brain damage, Reversible Posterior Leukoencephalopathy Syndrome, which may cause headache, seizure, blindness
- Severe blood infection
- Anemia, kidney problems which may require dialysis
- Blood clot
- Blockage of the airway which may cause cough

<u>Risks of Docetaxel</u>

Likely

- Swelling of the body
- Hair loss
- Change in nails
- Rash, itching
- Vomiting, diarrhea, nausea, constipation
- Sores in mouth which may cause difficulty swallowing
- Infection, especially when white blood cell count is low
- Anemia which may require blood transfusions
- Bruising, bleeding
- Tiredness
- Numbness and tingling of the arms and legs
- Fever
- Absence of menstrual period
- Swelling and redness of the arms, leg or face
- Pain
- Watering, itchy eyes

Less Likely

- Severe skin rash with blisters and peeling which can involve inside of mouth and other parts of

the body
- Belly pain
- Kidney damage which may require dialysis
- Blood clot which may cause swelling, pain, shortness of breath
- Abnormal heart rate
- Shortness of breath, wheezing
- Chest pain

Rare and Serious
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Cancer of bone marrow (leukemia) caused by chemotherapy

Please be aware that docetaxel may cause you to become intoxicated from the alcohol it contains. You should avoid driving, operating machinery, or performing other activities that are dangerous within one to two hours after the infusion of docetaxel. In addition, some medications, such as pain relievers and sleep aids, may interact with the alcohol in the docetaxel infusion and worsen the intoxicating effects.

Risks of Blood Draw
Possible side effects from a blood draw include fainting, feeling dizzy, pain, swelling, bruising, or bleeding where the needle is inserted. There is also a slight possibility of infection where the needle is inserted.

Risks of Tumor Biopsy
Your doctor will inform you in detail about the risks associated with biopsy. The level of risk will depend on where the tumor is located. In general, having a biopsy can cause pain, swelling, bleeding, and/or infection at the site where the biopsy penetrates through the skin. There is also the possibility that having this procedure may shift some cells from the tumor into the surrounding tissues that come in contact with the biopsy needle. This means that the tumor may spread to that particular area. Depending on the area of the biopsy, a local anesthetic (to numb the area) may be injected into the skin, or a sedative medication may be given orally or intravenously. The risks of this anesthetic are minimal and include bleeding, bruising, infection, and allergic reaction. The risks associated with use of a sedative are similar, but also include drowsiness, slurred speech, staggering gait, poor judgment, and slowed reflexes.

Risks of ECG
The risks can include skin irritation and a rash due to wearing and the removal of the electrodes. The electrodes only detect electrical impulses produced by the heart. No electricity passes through the body from the machine, and there is no danger of getting an electrical shock.

Risks of CT Scan
CT scans involve exposure to radiation. Although the amount of radiation exposure is higher than a typical x-ray, the risk of harmful effects from a single exam is very small. If you are scheduled for a CT with contrast, the dye that is injected into a vein for the scan is usually well tolerated. Some people feel dizzy, queasy, or get a headache when given the dye or notice a cold feeling near the injection site.

There is a rare chance of having an allergic reaction to the dye that very rarely can be serious or life threatening. You must tell your doctor if you have had bad reactions to dyes before. There is also a rare chance that a CT scan may cause a malfunction of worn or implanted medical devices. If you wear or have electronic medical devices such as a pacemaker or a drug pump, please make sure you tell your study doctors and research staff.

Risks of Radiation Exposure

This research involves exposure to radiation from CT scans. Because of your condition, which may limit your life expectancy, there is little or no risk to you from the radiation exposure in this study. If you would like more information about radiation exposure, please see the "Radiation Fact Sheet" located at http://hrpo.wustl.edu/ or ask the study staff for a copy.

Because certain research studies are subject to specific radiation exposure limits, it is important that you inform us if you have been in any other research studies in the last 12 months that involved exposure to radiation for research purposes (from x-rays, CT scans, PET scans or other nuclear medicine procedures). It is also important that you tell future investigators about your participation in this research study if you are asked to participate in another research study.

Risks for Women Capable of Becoming Pregnant

If you are a woman capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study. You must use effective birth control methods and try not to become pregnant while participating in this study. If you become pregnant, there may be unknown risks to your unborn child, or risks to your unborn child that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to an unborn child. You must tell the doctor if your birth control method fails while you are on the study. If you believe or know you have become pregnant while participating in this research study, please contact the research team member identified at the top of this document as soon as possible. Please discuss with the research team how long you need to wait before becoming pregnant after completing the treatment or procedures on this study.

Risks of Radiation Exposure in Women Capable of Becoming Pregnant

You may not participate in this study if you are pregnant. If you are capable of becoming pregnant, we will perform a pregnancy test before exposing you to research-related radiation. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time.

Risks for Sexually Active Male

If you are a sexually active male, it is important that your partner not become pregnant during your participation in this study. There may be unknown risks to the unborn child or risks we did not anticipate. You and your partner must agree to use birth control if you want to take part in this study. If you believe or know that your partner has become pregnant during your participation in this study, please contact the research team member identified at the top of this document as soon as possible.

Risks of Genetic Research

There may be information obtained from the future genetic research that indicates that you, or potentially a family member (since we inherit genes from our parents, and pass genes on to our children)

are at risk for a particular disease or condition. For example, genetic sequencing may indicate that an individual is more prone to develop certain types of cancer or other types of neurological disease, (e.g. Alzheimer's).

If made available to persons or agencies outside of our research group, information about genetic test results could affect your employment or insurance. For instance, employers, insurers, or others may use this information when making decisions about you or your family members regarding employment, insurance, or other benefits.

There is a federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans and employers with greater than 15 employees to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance or long term-care insurance.

Risk of Re-Identification from Genetic Research

While the data developed for this study is being stored without traditional identifiers (stored only with coded ID numbers, no names), there may be ways of linking the genetic materials back to you. DNA does directly identify you, so it is possible that someone could compare information in our database with information from you in another database and be able to identify you.

Risks of Breach of Confidentiality

One risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure. Please see the section in this consent form titled *"How will you keep my information confidential?"* for more information.

WHAT ARE THE BENEFITS OF THIS STUDY?

You may or may not benefit from being in this study. However, we hope that, in the future, other people might benefit from this study because it will help researchers learn more about using ADI-PEG 20 as part of the treatment for soft tissue sarcoma.

WHAT OTHER TREATMENT OPTIONS ARE THERE?

Before you decide whether or not to be in this study, your doctor will discuss the other options that are available to you. Instead of being in this study, you could:

- Get treatment or care for your cancer without being in a study;
- Take part in another research study;
- Get no treatment;
- Get comfort care, also called palliative care, which helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer without treating the cancer directly.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

As part of this study you will receive tests and procedures that are similar to what you would receive during routine clinical care of your condition. Your health plan/insurance company will be billed for some or all of these costs, and you will be responsible for any co-pays and deductibles that are normally required by your health plan/insurance. Not all insurance plans cover the costs associated with being in

a study. Even if they do, you may be responsible for more out-of-pocket expenses, such as co-pays and deductibles, when there are more tests and procedures or more expensive tests and procedures involved in the study than if you were to receive routine clinical care outside the study.

If you wish to know whether there are more tests and procedures or more expensive tests and procedures in the study, you should ask your study doctor.

If you wish to know whether your insurance will pay, you should contact them directly, or speak with the study team about obtaining a financial pre-certification prior to enrolling in the study.

Polaris Pharmaceuticals is providing the ADI-PEG 20 at no cost to you.

WILL I BE PAID FOR PARTICIPATING?
You will not be paid for being in this research study.

WHO IS FUNDING THIS STUDY?
Polaris Pharmaceuticals is providing the ADI-PEG 20 for this research study. No one on the research team will receive a direct payment or increase in salary from Polaris Pharmaceuticals for conducting this study.

The National Institute of Health (NIH) is also funding this research study. This means that Washington University is receiving payments from the NIH to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from the NIH for conducting this study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?
Washington University investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator at (314) 362-7997 and/or the Human Research Protection Office at 1-(800)-438-0445.

Decisions about whether payment for medical treatment for injuries relating to your participation in research will be made by Washington University and Polaris Pharmaceuticals. If you need to seek medical care for a research-related injury, please notify the investigator as soon as possible.

HOW WILL YOU KEEP MY INFORMATION CONFIDENTIAL?
Other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you. We will keep your participation in this research study confidential to the extent permitted by law.

- Government representatives (including the Office for Human Research Protections) to complete federal or state responsibilities
- The National Institutes of Health (NIH), which is funding a portion of this study
- The U.S. Food and Drug Administration
- Polaris Pharmaceuticals, manufacturer of ADI-PEG 20
- Your primary care physician if a medical condition that needs urgent attention is discovered

- Public health agencies to complete public health reporting requirements
- Hospital or University representatives to complete Hospital or University responsibilities
- Information about your participation in this study may be documented in your health care records and will be available to anyone with access to your health care record, including your health insurance company. This information may also be released as part of a release of information request.
- The last four digits of your social security number may be used in hospital or University systems to track billing information for research procedures.
- Washington University's Institutional Review Board (a committee that oversees the conduct of research involving human participants) and the Human Research Protection Office. The Institutional Review Board has reviewed and approved this study.

The research team will send study results to Polaris. Information sent to Polaris will be de-identified. In the future, Polaris may continue to use your health information that is collected as part of this study. For example, Polaris may combine information from this study with the results of other studies to re-analyze the safety and effectiveness of the study medication, to evaluate other products or therapies, to develop a better understanding of a disease, or to improve the design of future research studies. Polaris may also share information from the study with regulatory agencies in foreign countries.

If you receive Medicare benefits, are injured as part of your participation in this research study and medical treatment relating to this injury is paid by anyone other than you or your insurance company, that payer will need to collect personal information about you. This information includes your name, date of birth, gender, social security number, Medicare identification number and information related to this research study. The payer will report this information to the Centers for Medicare & Medicaid Services (CMS), the federal agency that oversees the Medicare program, during your participation in the study and for as long as the payer is required by CMS to report this information. If you do not want to release your personal or treatment related information you have the right to refuse reimbursement by the payer for any research injury. The payer will not use this information for any other purpose.

The Siteman Cancer Center at Washington University School of Medicine and Barnes-Jewish Hospital is supported by funding from the National Cancer Institute (NCI). To meet NCI requirements, your protected health information relating to your participation in this study (including your social security number) will be stored in a secure database at the Siteman Cancer Center. This database and also your health care records may be reviewed by Siteman Cancer Center personnel. All information will be securely and confidentially maintained.

To help protect your confidentiality, we will store paper records (those containing identifiers and those that are de-identified) in a locked office in a locked suite and we will store electronic records (which will contain identifiers) in a password-protected database on a secure server. Biologic specimens taken as part of this study will be stored with a linked code number as ID in a locked room accessible by WU swipe card. Any report or article that we write will not include information that can directly identify you. The journals that publish these reports or articles require that we share your information that was collected for this study with others. Sharing this information will allow others to make sure the results of this study are correct and help develop new ideas for research. Your information will be shared in a way that cannot directly identify you.

To further protect your privacy, this research is covered by a Certificate of Confidentiality from the federal government. This means that the researchers can refuse to disclose information that may identify you in any legal or court proceeding or to anyone who is not connected with the research except if:

- there is a law that requires disclosure, such as to report child abuse and neglect, or harm to self or others*;*
- you give permission to disclose your information, including as described in this consent form; or
- it is used for other scientific research allowed by federal law.

You have the right to share your information or involvement in this study with anyone at any time. You may also give the research team permission to disclose your information to a third party or any other person not connected with the research.

If information about you or your involvement in this research is placed in your medical record the information may no longer be protected under the Certificate. However, information in your medical records is protected in other ways.

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Are there additional protections for my health information?

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form. The research team will follow state and federal laws and may share your health information with the agencies and people listed under the previous section titled, "How will you keep my information confidential?"

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form or as permitted or required by law. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have questions or concerns about your privacy and the use of your PHI, please contact the University's Privacy Officer at 866-747-4975.

Although you will not be allowed to see the study information, you may be given access to your health care records by contacting your health care provider.

If you decide not to sign this form, it will not affect

- your treatment or the care given by your health provider.
- your insurance payment or enrollment in any health plans.
- any benefits to which you are entitled.

However, it will not be possible for you to take part in the study.

If you sign this form:

- You authorize the use of your PHI for this research
- This authorization does not expire.
- You may later change your mind and not let the research team use or share your information (you may revoke your authorization).
  - To revoke your authorization, complete the withdrawal letter, found in the Participant section of the Human Research Protection Office website at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ or you may request that the investigator send you a copy of the letter.
    - **If you revoke your authorization:**
      - The research team may only use and share information already collected for the study.
      - Your information may still be used and shared as necessary to maintain the integrity of the research, for example, to account for a participant's withdrawal from the research study or for safety reasons.
      - You will not be allowed to continue to participate in the study.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. Any data that was collected as part of your participation in the study will remain as part of the study records and cannot be removed.

If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I decide to withdraw from the study?

You may withdraw by telling the study team you are no longer interested in participating in the study or you may send in a withdrawal letter. A sample withdrawal letter can be found at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ under Withdrawing from a Research Study.

If you decide to leave the study early, we will ask you to tell the study doctor if you are thinking about stopping so any risks can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

Will I receive new information about the study while participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can someone else end my participation in this study?

Under certain circumstances, the investigator might decide to end your participation in this research study earlier than planned. This might happen for no reason or because staying in the study would be harmful, you need treatment that is not allowed while on the study, you fail to follow instructions, you

become pregnant, you develop a major side effect, or the study is canceled.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact Dr. Van Tine at (314) 362-7997. If you experience a research-related injury, please contact Dr. Van Tine as well; if this is after hours, you will be directed to the exchange number which will be covered by a resident or fellow on call. Please tell this person that you are a research participant.

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office at 660 South Euclid Avenue, Campus Box 8089, St. Louis, MO 63110, 1-(800)-438-0445, or email hrpo@wustl.edu. General information about being a research participant can be found on the Human Research Protection Office web site, http://hrpo.wustl.edu. To offer input about your experiences as a research participant or to speak to someone other than the research staff, call the Human Research Protection Office at the number above.

This consent form is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by agreeing to participate in this study. As a participant you have rights and responsibilities as described in this document and including:

- To be given enough time before signing below to weigh the risks and potential benefits and decide if you want to participate without any pressure from the research team or others.
- To understand all of the information included in the document, have your questions answered, and receive an explanation of anything you do not understand.
- To follow the procedures described in this document and the instructions of the research team to the best of your ability unless you choose to stop your participation in the research study.
- To give the research team accurate and complete information.
- To tell the research team promptly about any problems you have related to your participation, or if you are unable to continue and wish to stop participating in the research study.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a signed and dated copy of this form.

Do not sign this form if today's date is after EXPIRATION DATE: 01/18/22.

_____ _____
(Signature of Participant) (Date)

_____
(Participant's name – printed)

Parent/Guardian Name and Relationship to Participant:

Do not sign this form if today's date is after EXPIRATION DATE: 01/18/22.

_____
(Child's name – printed)

_____ _____
(Signature of Parent/Guardian) (Date)

_____ _____
(Name of Parent/Guardian- printed) (Relationship to participant – printed)

Second Parent/Guardian Name and Relationship to Participant:

Do not sign this form if today's date is after EXPIRATION DATE: 01/18/22.

_____
(Child's name – printed)

_____ _____
(Signature of Parent/Guardian) (Date)

_____ _____
(Name of Parent/Guardian- printed) (Relationship to participant – printed)

Statement of Person Who Obtained Consent

The information in this document has been discussed with the participant or, where appropriate, with the participant's legally authorized representative. The participant has indicated that they understand the risks, benefits, and procedures involved with participation in this research study.

_____ _____

(Signature of Person who Obtained Consent) (Date)

_____

(Name of Person who Obtained Consent - printed)