APPENDIX F: SAMPLE INFORMED CONSENT

PROTOCOL M18-006: YOSEMITE: A 3-Arm Phase 2 Double-Blind Randomized Study of Gemcitabine, Abraxane® Plus Placebo versus Gemcitabine, Abraxane® plus 1 or 2 Truncated Courses of Demcizumab in Subjects with 1st-line Metastatic Pancreatic Ductal Adenocarcinoma

Principal Investigator: _____

Before you decide whether or not to take part in this research study, it is important for you to understand the purpose of the study, what risks may be involved, and what is expected of you during the study. If you have any questions that are not answered or if there are words that you do not understand in this consent form, a member of the research team will give you further information. Once you understand the purpose of this study, and if you decide to volunteer to participate in the study, you will be asked to sign this consent form.

You are being asked to participate in this research study because you have been diagnosed with 1st-line Metastatic Pancreatic Ductal Adenocarcinoma.

PURPOSE AND BACKGROUND

Current cancer therapies often produce an initial reduction in tumor size but may not have long-term benefits. One possible explanation for this is the presence of a specific type of cancer cell known as a cancer stem cell. Cancer stem cells represent a small part of the tumor but are believed to be responsible for much of the growth and spread of the cancer. Cancer stem cells may also be more resistant to traditional types of therapy, such as chemotherapy and radiation therapy.

The purpose of this study is to compare the efficacy and safety of 1 or 2 truncated courses of a new experimental drug, demcizumab, when given in combination with gemcitabine and Abraxane® to gemcitabine and Abraxane (plus placebo). The administration of Gemcitabine and Abraxane® is a standard treatment for subjects with pancreatic cancer. You also may be given antiemetic therapy and/or hematopoietic growth factors and/or red blood cell/platelet transfusions, if your study doctor considers it appropriate

Demcizumab is a humanized monoclonal antibody and was developed to target cancer stem cells. Demcizumab may block the growth of cancer stem cells, the remaining cancer cells, and it may also prevent the growth of new blood vessels that tumors need to grow and spread. Demcizumab, used in this study, is experimental. That means that the United States Food and Drug Administration (FDA) has not approved it for use by the general public. This study is sponsored by OncoMed Pharmaceuticals, which is referred to as OncoMed or the Sponsor in this consent form.

WHAT IS EXPECTED FROM YOU?

- When deciding whether to participate, consider whether you are able and willing:
- To follow the study rules
- To commit the time required to keep appointments
- To tell the study doctor truthfully about your complete medical history
- To report any new problems, illnesses, or changes in medication during the study

PROCEDURES

Up to 201 subjects will be enrolled at up to 65 centers in North America, Western Europe, and Australia. Up to 28 days (4 weeks) prior to treatment you will undergo testing to determine your eligibility to take part in this study.

If enrolled in the study you will receive intravenous (in the vein) infusions of the demcizumab (or placebo) once every 2 weeks for the duration defined by your treatment group stated in the next section. Abraxane® and Gemcitabine will be administered on Days 1, 8 and 15 of each 28-day treatment cycle and will continue until toxicity necessitates reducing or holding a dose). The treatment arms are defined in the next section. If your physician decides to delay treatment with one of the agents due to side effects, the other agents may still be administered as scheduled. You will undergo assessments every 8 weeks to determine the status of your *disease* and for safety at every visit and through 30 days following the termination of study drug

In addition to routine testing of blood and urine (for complete blood counts with differential and platelets, coagulation studies to determine how quickly your blood is clotting; serum chemistries; and B-type natriuretic peptide [BNP], which indicate how well your heart if working; creatinine clearance to measure your kidney function and urinalysis), special tests will be performed during the study at specific time points listed below. The samples for special tests will be sent to OncoMed Pharmaceuticals, 800 Chesapeake Dr., Redwood City, California, U.S.A, 94063 The special tests include the following:

- Tumor markers: These are substances that can be detected in higher than normal amounts in blood, urine, or body tissues for certain types of cancer. The tumor marker level may indicate the extent of the cancer in your body and may show how you are responding to treatment. For this study, only blood samples will be taken to check for tumor markers. The tumor marker for pancreatic cancer is: CA 19-9. If your baseline: CA 19-9 tumor marker is not elevated, the test will not be repeated during the study.

- Antibodies to demcizumab: Antibodies are proteins produced by your body's immune system in response to a foreign substance. In some cases, the development of antibodies to a treatment will not have any impact on the effectiveness of the treatment. In other cases, the development of antibodies to a treatment can cause the treatment to be

ineffective. Blood will be drawn, , at baseline and then every 8 weeks, and at treatment termination, to determine if you are developing antibodies to demcizumab. . The anti-demcizumab antibody samples will be sent to ICON, [redacted].

- Pharmacokinetic Analysis: Blood samples will be obtained prior to your demcizumab (or placebo) infusion on Study Days 0, 14, 56, 70, 168, 182, 224 and 238, and at the end of the demcizumab infusion (prior to chemo infusion) on Days 0, 56, 70, 168, 224 and at treatment termination visit to determine how the demcizumab is distributed and eliminated from your body. The PK samples will be sent to ICON, [redacted].

- Biomarkers: At specified time points blood samples will be obtained to assess whether the demcizumab is producing desired changes to the genes and proteins related to your cancer. A predose sample of 9 mL of blood will be drawn on Study Days 0, 21, 35, 49 and 63 and at treatment termination.

- In addition, archival tumor tissue sections (formalin-fixed paraffin-embedded (FFPE)) will be collected if available for gene and protein testing of biomarkers related to your cancer.If you agree to have DNA testing on your FFPE tissue, you will sign a separate consent. DNA testing of your tumor may help to identify biomarkers that could be used in the future to predict which patients are more likely to respond to demcizumab, gemcitabine and Abraxane treatment.

In addition, you will have an ECG and doppler echocardiogram performed during screening, then every 28 days on study and at treatment termination. Your Doppler echocardiograms may be sent to a Cardiologist at another hospital who may perform a central read on some of the doppler echocardiograms in this study. Finally, you will have a head CT or MRI at baseline and CT scans and/or other radiographs performed every 56 days to assess the status of your tumor. A CT pulmonary angiogram (CTPA) (or MR angiogram or VQ scan if you have an allergy to the contrast dye) may be performed if you are diagnosed with pulmonary hypertension to see if you might have a pulmonary embolism.

SCREENING

If you volunteer to be in this study and you sign this informed consent form, you will be screened within 28 days before study entry to make sure that you are a suitable candidate. No study-related tests will be performed prior to signing this informed consent form. Results of your standard of care tests or examinations before signing this informed consent form and within 28 days prior to Day 0 may be used for screening assessments rather than repeating such tests. Your doctor will:

- Conduct a review of your physical health and medical history, including a review of any medications you are or have been taking.
- Conduct a physical exam including height and weight will be performed, Peripheral neuropathy assessment and vital signs including your pulse, blood pressure, breathing rate and temperature will be measured.
- Collect blood and urine samples for routine testing.
- Collect blood for testing of tumor markers. Approximately 3 tablespoons of blood will be taken at this visit.
- Complete an electrocardiogram (ECG), doppler echocardiogram, and either a computerized tomography (CT) scan or magnetic resonance imaging (MRI) of your chest, abdomen, pelvis, and head.
- Order a colonoscopy and/or upper gastrointestinal endoscopy if your tumor involves your esophagus, stomach, or intestinal tract or if you have symptoms that suggest that that your tumor may involve these areas, to ensure that your tumor does not currently involve your gastrointestinal tract.
- Complete a serum pregnancy test within 7 days prior to the first dose of demcizumab if you are a female of childbearing potential, to ensure that you are not pregnant at the start of the study.

TREATMENT PHASE

Demcizumab (or Placebo)

Once your doctor has evaluated the results of your screening tests to ensure that you meet the criteria for the study and are eligible to participate, you will be randomized in the study and assigned to a treatment arm.

You will receive 3.5 mg/kg demcizumab or placebo as shown in the treatment arms, below. A placebo looks like the demcizumab, but does not contain any medication. Dosing of Gemcitabine, Abraxane® and Demcizumab or placebo must be done within ± 2 days of the Study Day listed in the protocol. If a drug cannot be given within this 2 day window, then the dose of that drug is permanently missed.

Demcizumab 3.5 mg/kg or placebo will be administered by IV infusion (prior to the administration of Abraxane® and Gemcitabine) once every 2 weeks for either one (1st course through Study Day 70) or two (2nd course begun on Study Day 168 and continued through Study Day 238) 70 day courses. You will receive 6 doses of demcizumab or placebo during the 1st 70 day course of treatment and an additional 6 doses of demcizumab or placebo during the 2nd

70 day course of treatment (beginning on Day 168). You will be randomly (by chance) assigned to one of the three treatment arms:

Arm 1:

- Abraxane® and gemcitabine plus **placebo** (3 cycles), then
- Abraxane® and gemcitabine (3 cycles), then
- Abraxane® and gemcitabine plus **placebo** (3 cycles), then
- Abraxane® and gemcitabine until disease progression

Arm 2:

- Abraxane® and gemcitabine plus **demcizumab** (3 cycles), then
- Abraxane® and gemcitabine (3 cycles), then
- Abraxane® and gemcitabine plus **placebo** (3 cycles), then
- Abraxane® and gemcitabine until disease progression

Arm 3:

- Abraxane® and gemcitabine plus **demcizumab** (3 cycles), then
- Abraxane® and gemcitabine (3 cycles), then
- Abraxane® and gemcitabine plus **demcizumab** (3 cycles), then
- and then Abraxane® and gemcitabine until disease progression

You will have an equal chance of being assigned to Arm 1, Arm 2 or Arm 3. Neither you nor your doctor will know which treatment arm you have been assigned, or whether you are receiving demcizumab or placebo.

Abraxane®

Abraxane® must be administered after the demcizumab, but before gemcitabine administration on days when three drugs are given. Abraxane® should be administered by IV infusion at a starting dose of 125 mg/m^2 over 30 minutes on Days 1, 8 and 15 of every 28-day cycle. The dose of Abraxane may be reduced over time if necessary to reduce toxicity.

Gemcitabine

Gemcitabine must be administered after the administration of demcizumab and Abraxane®. Gemcitabine should be administered by IV infusion at a starting dose of 1000 mg/m^2 over

30 minutes once weekly for 3 weeks (or until toxicity necessitates reducing or holding a dose), followed by a week of rest every 28 days. The dose of gemcitabine may be reduced over time if necessary to reduce toxicity.

Study Day 0: This is considered your randomization visit where you will start your study treatment. This visit will take approximately (3) hours. The following assessments will be done prior to the infusion of demcizumab or placebo, Abraxane®, and Gemcitabine: abbreviated physical examination including weight; Peripheral neuropathy assessment review of medications you are taking, including any changes in medication since the screening visit; changes in your medical status; and vital signs. Approximately 4 tablespoons of blood will be drawn for routine tests, antibody testing, pharmacokinetic testing (before and after your infusion) and biomarkers.

Study drug will be administered and you will be monitored for at least 15 minutes after the demcizumab (or placebo) has been stopped. Abraxane® will then be administered, followed by Gemcitabine.

- **Study Days 7, 14, 21, 28, 35, 42, and 49:** demcizumab or placebo will be given on Days 14, 28 and 42 only, Abraxane®, and Gemcitabine will be given on Study Days 7, 14, 28, 35 and 42 only. The following assessments will be obtained weekly: weight; review of the medications you are taking and any changes in medication since the previous visit; changes in your medical status or new health problems since the previous study visit; and vital signs. An abbreviated physical examination will be performed on the days that your receive demcizumab or placebo, and also your BNP will be measured those days. At Day 28 only, Peripheral neuropathy assessment

Blood will be taken for routine testing. On Day 28, blood will be taken before the infusion of demcizumab (or placebo), for pharmacokinetic testing. At Day 21, Day 35 and Day 49, blood will also be obtained for biomarkers. Approximately 3 tablespoons of blood will be drawn on Study Days 7, 14, 21, 28, 35, and 42.

- At Day 28 only, a urine specimen will be obtained for routine testing. On Day 28, an ECG and doppler echocardiogram will be done.

Study Day 56: The following assessments will be obtained on Day 56: weight; review of medications you are taking and any changes in medication since the previous visit; changes in your medical status or new health problems since the previous study visit; and vital signs and abbreviated physical exam BNP measured, urine specimen for routin*e* testing, Peripheral neuropathy assessment.

Blood will be obtained for routine testing, pharmacokinetics, immunogenicity and if you are a female of child-bearing potential for a serum pregnancy test. Approximately 3 tablespoons of blood will be drawn during this visit. An ECG and doppler echocardiogram will be done. Tumor marker: CA 19-9 (if elevated at baseline) will be done, In addition, on Day 56, you will undergo a CT scan or MRI of the chest, abdomen, and pelvis, to assess whether your cancer has

improved, progressed, or is stable. If the CT scan or MRI shows that you have stable or improved disease, you may continue to receive demcizumab, Abraxane®, and Gemcitabine

If the CT scan or MRI shows disease progression, you will be taken off the study and will undergo assessments listed under **Treatment Termination**. At this point, your study doctor will discuss alternate treatment options.

Study Days 63 and 70: demcizumab or placebo, will be given on Day 70 only, Abraxane®, and Gemcitabine will be given on Day 63 and 70. The following assessments will be obtained prior to the infusion of drug: weight; review of the medications you are taking and any changes in medication since the previous visit; changes in your medical status or new health problems since the previous study visit; and vital signs. An abbreviated physical examination will be performed on the day that your receive demcizumab (or placebo).

Blood will be taken for routine testing, blood will also be taken for biomarkers on day 63, and blood will also be taken for pharmacokinetics on day 70. Approximately 3 tablespoons of blood will be drawn on Study Days 63 and 70. BNP will be also measured

Study Day 77: The following assessments will be obtained: weight; review of the medications you are taking and any changes in medication since the previous visit; changes in your medical status or new health problems since the previous study visit; and vital signs. Approximately 3 tablespoons of blood will be taken for routine testing. An abbreviated physical examination will be performed

Study Days 84, 91 and 98: Abraxane®, and Gemcitabine. The following assessments will be obtained: weight; review of the medications you are taking and any changes in medication since the previous visit; changes in your medical status or new health problems since the previous study visit; Peripheral neuropathy assessment (Day 84 only) ,and vital signs. An abbreviated physical examination will be performed on Days 84 and 98 only, and BNP measured on Days 84 and 98 only.

Blood will be taken for routine testing. On Study Day 84 only, blood will also be obtained for testing for antibody formation to demcizumab. Approximately 3 tablespoons of blood will be drawn on Study Days 84, 91, and 98.

On Day 84 only an ECG and doppler echocardiogram will be done.

Study Day 105: The following assessments will be obtained weight; review of the medications you are taking and any changes in medication since the previous visit; changes in your medical status or new health problems since the previous study visit; and vital signs.

Approximately 3 tablespoons of blood will be taken for routine testing.

As long as your disease is stable or shows a response, you may continue to be treated. You will undergo the tests listed for Study Days 84, 91, 98, and 105. In addition, every 8 weeks you will

undergo a CT scan or MRI of the chest, abdomen, and pelvis, to assess whether your cancer has improved, progressed, or is stable.

In addition, every 8 weeks blood will be obtained for tumor markers, if applicable and if you are a female of child-bearing potential for a serum pregnancy test. You will also have a doppler echocardiogram every 4 weeks.

TERMINATION VISIT

When your tumor has progressed or you are going to be removed from the study for another reason the following assessments will be performed: abbreviated physical exam with weight; review of medications you are taking and any changes in medication since the previous visit; changes in your medical status or new health problems since the previous study visit; Peripheral neuropathy assessment and vital signs.

Blood samples will be obtained for routine testing (including BNP), antibody formation to demcizumab, pharmacokinetic testing, and biomarkers unless obtained within the previous 14 days. Blood will also be obtained for tumor marker testing if applicable and for BNP unless obtained within the previous 28 days. In addition, if you are a female of child-bearing potential, blood will be obtain*ed* for a serum pregnancy test. A urine specimen will be obtained unless one was obtained within 28 days of treatment termination. An ECG will be done and a doppler echocardiogram will be performed. A repeat CT scan or MRI of the chest, abdomen, and pelvis will be obtained unless performed within 7 days of termination visit.

Approximately 3 tablespoons of blood will be drawn during this visit.

FOLLOW-UP AFTER TERMINATION VISIT

If your blood pressure was too high at the Termination visit (greater than 150/90 mmHg), your blood pressure will be determined every 2 weeks until your blood pressure is less or equal to 150/90 mmHg for a 4-week period.

If you are a female of child-bearing potential, you will have a serum pregnancy test done 56 and 112 days after your termination visit.

You will be contacted every 3 months for up to 5 years by the clinic study staff to check on your condition. This contact may be by telephone or medical record review. Information regarding any anti-cancer therapies that you receive will also be collected through telephone calls, review of medical records, and/or clinic visits.

In addition, if your tumor has not progressed at the time of your Termination visit, your tumor response outcome will continue to be followed until you begin receiving alternative anti-cancer treatment or your tumor progresses, whichever occurs first, and a copy of the corresponding radiographs (e.g., CT scans and/or MRIs) may be provided to OncoMed, the Sponsor of the trial. If you have a BNP greater than 400 pg/mL and/or a diagnosis of pulmonary hypertension or

heart failure at the time of termination, all subsequent standard of care BNP data will be collected until the value is less than or equal to 200 pg/mL and all subsequent standard of care left ventricular ejection fraction (LVEF) and peak tricuspid velocity (PTV) values will be collected until they normalize. LVEF and PTV are tests that provide information on how your heart is functioning. Below is a table that summarizes the treatment and tests that will be performed through Day 105. Similar testing will continue to be performed after Day 105 until you are removed from the study.

Day(s)	-28 to 0	0	7	14	21	28	35	42	49	56	63	70	77	84	91	98	105	Termination Visit	Follow-up after termination visit
Informed consent Past medical history/ height/INR/aPTT Serum pregnancy test Head CT or MRI FFPE (if tissue blocks available) Colonoscopy and/or upper GI endoscopy (in subjects having symptoms of possible gastrointestinal involvement)	X																		
Abraxane/ Gemcitabine		X	X	X		X	X	X		X	X	X		X	X	X			
Demcizumab or placebo		X		X		X		X		X		X							
Physical exam	X	X		X		X		X		X		X		X		X		X	
Weight and vital signs/ ECOG performance status	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Concomitant meds/ Adverse event evaluation		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
CBC w/diff, plts/ Serum Chemistry	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
BNP	X			X		X		X		X		X		X		X		X	
Peripheral neuropathy assessment	X	X				X				X				X				X	
Anti-demcizumab antibody/ ECG/ Transthoracic doppler echocardiogram	X					X				X				X				X[t]	
Urinalysis	X					X				X								X	
Tumor marker CA 19-9 Chest, abdomen, and pelvis radiographic evaluation	X									X								X	
Blood for biomarkers		X			X		X		X		X							X	
Pharmacokinetics		X		X						X		X						X	
Optional Pharmacogenomics		X																	
Survival data including date and cause of death) Subsequent anti-cancer therapiesy Response assessment data																			X

POSSIBLE RISKS AND DISCOMFORTS

You may have side effects while you are in the study, but you will be carefully checked by the study doctor for any problems. There may be risks or side effects of the study treatment that are unknown at this time. You should tell the study doctor/staff about anything that is bothering you or any side effects you have, even if you do not think they are related to the study drug.

The following is a list of the most medically significant or most common side effects reported in completed studies of demcizumab, Abraxane® and/or gemcitabine. In some cases, side effects can be serious, long-lasting, or can cause death. Some side effects go away soon after you stop the study treatment/therapy and some may never go away. The study doctor may alter the dosage regimen of one or more of these drugs (if allowed by the study) or give you medicines to help lessen the side effects. This is not a complete list of all side effects that may occur. For more information about risks and side effects, please ask the study doctor.

Demcizumab

The following are the side effects that were observed in >10% (common) and 5-10% (less common) of the 55 patients treated in the initial **single-agent study** of demcizumab and were considered to be possibly related to demcizumab.

Common (occurred in >10% of patients who received demcizumab)

Hypertension, fatigue, anemia, diarrhea, headache, nausea, decreased protein in the blood and shortness of breath

Less Common (occurred in 5-10% of patients who received demcizumab)

Low sodium in blood, dizziness, weight loss, heart failure, laboratory values indicating a decrease in liver or kidney function, decreased white blood count in the blood, abdominal pain, chills, fever, insomnia and cough

The following are the side effects that were observed in >10% (common) and 5-10% (less common) of the 99 patients treated in the 4 studies of **demcizumab plus chemotherapy** and were considered to be possibly related to demcizumab.

Common (occurred in >10% of patients who received demcizumab and chemotherapy)

Fatigue, nausea, hypertension, swelling of tissue due to increased fluid, diarrhea, appetite decreased, increased BNP (suggesting possible early damage to the heart), anemia, decreased platelet count in the blood, decreased white blood count in the blood, shortness of breath, headache, increased pressure in the lungs, constipation and rash.

Less Common (occurred in 5-10% of patients who received demcizumab and chemotherapy)

Change in taste, hair loss and laboratory values indicating a decrease in liver function

The majority of the side effects observed in these studies were mild to moderate. The most common adverse event across these studies that was clearly related to demcizumab was hypertension which occurred in 14-60% of the patients. Thus, if you participate in this study, your blood pressure will be checked frequently and, if necessary, you will be treated with medication(s) to lower your blood pressure. If your increased blood pressure is not controlled by medications, administration of demcizumab will be discontinued.

In addition, in these studies, 7 patients developed serious bleeding in the gastrointestinal tract. Two patients died as a result of this bleeding. Because of that, you will not be treated in this study if you have tumor in one or more locations that carries an increased risk for bleeding. If you participate in the study, your hemoglobin (a measurement of the amount of red blood cells) will be tested regularly. If your hemoglobin decreases, your physician will look carefully for the reason. If you develop active significant bleeding, administration of demcizumab will be discontinued.

One patient in the single-agent study died as a result of complications relating to a tumor within the brain. As a result, if you choose to participate in this study, prior to treatment you will have a scan of the brain to ensure that there is no tumor within the brain. Patients who have a tumor within the brain will not be able to participate in the study.

Finally, approximately 40% of patients treated in these trials developed rises in a laboratory test (BNP) suggesting possible early damage to their heart. In addition, approximately 5-10% of the patients had symptoms of heart failure (such as shortness of breath and/or extra fluid in their legs). These patients typically improved after discontinuation of demcizumab and treatment with medications to reduce their symptoms. In addition, the heart failure typically developed in patients who received demcizumab for at least 3 months. Also, an increase in the blood pressure in the lungs which can also result in heart failure has been observed in some patients that were typically treated for more than 3 months. As a result, demcizumab will not be given on an ongoing basis in this study. Instead, a shortened regimen of 6 doses over 70 days will be administered either once or twice during your time on study. Approximately 50 patients have received this type of shortened treatment schedule, and none have developed serious heart failure or increased blood pressure in the lungs. However, it is anticipated that heart failure and /or increased blood pressure in the lungs will likely still occur in some patients receiving this shortened duration of treatment with demcizumab. Finally, no patients have been previously treated with a 2nd 70-day course of demcizumab that some patients will be receiving in this study, so the risks of this approach are unknown.

You will not be treated in this study if you have an elevated BNP value, evidence of heart failure or evidence of disease in the vessels in your heart, or have a significant decrease in the amount of

blood your heart is pumping on Doppler echocardiogram. Your heart and lung function will be watched closely while you are on study using blood tests and echocardiograms. If these side effects are noted, you will be referred to a heart specialist who may be able to treat the side effects with drugs. If further increases in your BNP occur or the amount of blood your heart is pumping declines further, your demcizumab therapy will be discontinued.

As with all antibody treatments, there is the possibility of an allergic reaction, such as fever, chills, rash, and/or hives associated with the infusion of demcizumab. Rarely, a severe or serious allergic reaction can occur during or following the administration of an antibody.

Not enough patients have yet been treated with demcizumab to fully understand the side effects that may be associated with this antibody. It is possible that you may receive a lower dose of gemcitabine and/or Abraxane® than you would have received if you were not participating on this study due to additional toxicities caused by demcizumab.

The following side effects have been observed in other drugs that have an anti-angiogenic effect (drugs that prevent the growth of new blood vessels that tumors need to grow and spread) and in other drugs that may inhibit the growth of cancer stem cells. It is not known if the administration of demcizumab will result in any of these findings:

- Gastrointestinal perforation sometimes associated with intra-abdominal abscess
- Diarrhea, weight loss, constipation, vomiting, abdominal pain, nausea, and fever
- Wound healing complications
- Hemorrhage including minor bleeding events such as nose bleeds or more serious, sometimes fatal bleeding events
- Arterial or venous thromboembolic events, including cerebral (brain) infarction, transient ischemic attacks (TIAs), myocardial infarction (MI), angina, and other sometimes fatal events
- Hypertension including episodes of severe increased blood pressure
- Neutropenia and/or infection
- Proteinuria (loss of protein through your kidneys)
- Congestive heart failure
- Diarrhea
- Rashes
- Somnolence (sleepiness)
- Fatigue
- Prolonged QT interval (irregular heart rhythm)

Abraxane®

Very common (a 10% or more chance that this will happen):

- anemia (a decrease in the number of red blood cells (which may make you feel weak or tired)
- low number of white blood cells with or without fever (that may make it easier get infections)
- a decrease in the number platelets, the cells that help your blood to clot (which may lead to unusual bleeding or bruising under the skin)
- constipation
- diarrhea
- nausea
- vomiting
- stomach pain
- pain, swelling or sores on the inside of the mouth
- neuropathy, a disorder of the nerves which can cause tingling or numbness, with weakness, or decreased sensation or movement
- dizziness
- headache
- feeling tired or weak
- pain (including muscle, joints, bone, and chest pain)
- swelling caused by fluid held in the tissues, especially of the ankles, feet or fingers
- fever
- chills
- decreased appetite
- change in taste
- weight loss
- difficulty sleeping
- depression
- cough
- shortness of breath
- hair loss
- rash, possibly red, bumpy or generalized
- itchiness
- changes in nails, including discoloration or separation from nailbed
- abnormal liver function test results
- dehydration (loss of water and minerals in the body)
- nose bleed

Common (between a 1% to less than 10% chance that this will happen):

- bone marrow depression which is a severe reduction of red or white blood cells and platelets (at nearly the same time) which can cause weakness, bruising, or make infections more likely
- infections, including pneumonia or of the lung, mouth, gallbladder, urinary tract, nail, or hair follicle, (which may be bacterial, fungal or viral)
- a very severe infection of the blood which may include a decrease in blood pressure
- inflammation of the lung passages
- thickening, inflammation or scarring in the lungs which may cause breathlessness, cough
- inflammation of the bowel causing abdominal pain or diarrhea
- blockage of the intestine
- trouble swallowing
- indigestion or upset stomach
- abnormal chemistry or electrolyte blood test results
- abnormal kidney function test results
- acute kidney failure
- blood in the urine
- lack of muscle coordination
- muscle weakness
- anxiety
- nasal congestion
- mouth or throat pain
- dry mouth, nose, and throat
- coughing up blood or bloody sputum
- blood clot in the lungs or in deep vein
- fluid in the chest cavity
- red or flushed skin
- dry skin
- hand-foot syndrome, involving reddening, swelling, numbness and peeling of palms and soles of feet
- high blood pressure
- low blood pressure
- faster heart beat
- watery eyes
- changes in vision or blurry vision
- infusion site reactions (described as discomfort, bleeding or bruising/swelling at the needle site, and in some instances infection or leaking of IV fluid outside of blood vessel into the surrounding tissue)
- localized swelling due to build up of lymph fluid

Uncommon (between a 0.1 to less than 1% chance that this will happen):

- a decrease in the heart's ability to pump blood to all parts of the body and possibly heart failure
- irregular or slow heart beat
- stopping of the heart
- allergic reaction (may include skin inflammation, rash, trouble breathing, trouble speaking, fever), sometimes fatal
- syndrome involving abnormal blood clotting, with decreased platelets, bruising (including tiny red or purple spots under the skin) and possibly leading to blood clots
- edema/swelling and cyst formation of the macular area of the retina
- irritation and redness of the thin membrane covering the eye
- inflammation of the cornea
- too much fluid in the body
- feeling unwell
- sleepiness
- scaly or peeling skin
- hives
- a loss of nerve function in the muscles of the face

Additional side effects observed during post-marketing surveillance of Abraxane, not otherwise noted above include:

- a loss of nerve function in the muscles of the face or the eyes
- lack of movement in the vocal cords with possible voice changes
- skin sensitivity to sunlight
- potentially life threatening skin rash with skin blistering
- skin or tissue damage from prior radiation therapy can become damaged again, when a person receives chemotherapy after having had radiation therapy. This is referred to as radiation recall and may involve redness, peeling, pain, and swelling. Skin changes have been noted to range from mild redness to tissue death. Radiation recall may also occur in the lungs and other internal organs.

Abraxane® in Combination with Gemcitabine

In subjects with metastatic pancreatic cancer, who received the combination of Abraxane® and gemcitabine, there may be an increase of blood infections. Contact your study doctor immediately if you develop a fever. Your study doctor will evaluate if your fever is an early sign of a serious infection, which may require treatment.

A particular lung illness, known as pneumonitis (thickening, inflammation or scarring in the lungs with breathlessness, or cough), appears to occur more often (4%) when the two drugs are given together. This lung illness requires early detection and treatment as it may be life-threatening or even fatal. Therefore, it is important that you promptly tell your study doctor if you have worsening shortness of breath, difficulty breathing, fever, or a dry cough (not productive), for further evaluation and possible treatment.

In addition, acute renal or kidney failure and hemolytic uremic syndrome (a syndrome involving abnormal blood clotting, with decreased platelets, bruising including tiny red or purple spots

under the skin, and possibly leading to blood clots) have been reported commonly and uncommonly, respectively, in combination of Abraxane® with gemcitabine.

Gemcitabine

clinically important side effects of gemcitabine

Very common (a 10% or more chance that this will happen):

- blood and protein in the urine
- fluid retention (swelling of the hands, feet or face)
- difficulty breathing

Uncommon (between a 0.1 to less than 1% chance that this will happen):

- acute kidney failure (which can include hemolytic uremic syndrome)
- severe hepatic toxicity (example: hepatic failure, hepatic veno-occlusive disease)
- severe pulmonary toxicity (example: interstitial pneumonitis, pulmonary edema, adult respiratory distress syndrome

Additional side effects observed during post-marketing surveillance of gemcitabine, not otherwise noted above include:

- posterior reversible encephalopathy syndrome (a very rare condition known as posterior reversible encephalopathy syndrome has occurred when gemcitabine is given alone or in combination with other chemotherapy medications. Therefore, you should tell your study doctor if you have one or more of the following symptoms; headache, abnormal shaking of body, sleepiness, increased blood pressure, feeling confused, abnormal vision including loss of vision, loss of muscle control or muscle weakness, numbness or tingling in extremities)
- capillary leak syndrome (A very rare condition known as capillary leak syndrome that causes leaking of fluid outside of blood vessels has occurred when gemcitabine is given alone or in combination with other chemotherapy medications. Therefore, you should tell your study doctor if you have one or more of the following symptoms: fatigue; lightheadedness or fainting; pain in arms, legs, or stomach or all over body; swelling in face or body; difficulty breathing; low blood pressure)
- pulmonary fibrosis (excess of fibrous tissue in the lung and a severe pulmonary toxicity)
- vasculitis (an inflammation of the small blood vessels described as pain, heat, and redness to the affected part of the body)
- gangrene (dying tissue due to lack of blood supply described as skin discoloration, severe pain, foul smelling leakage from a sore, and may include swelling, and increased temperature to the affected region of the body)

You should inform your study doctor if you are planning any dental work while on study, as some study subjects have an increased risk of bleeding. It may be advisable to use a soft-bristled tooth-brush and to be careful when using dental floss and toothpicks.

Infusions:

Demcizumab or placebo, Abraxane and Gemcitabine will be given as intravenous infusions. There may be minor discomfort from the needle in your arm. Bruising, swelling and, in rare instances, infection and blood clot may occur at the infusion site.

Blood Draws:

During the course of this study, your blood will be drawn for laboratory tests (3-4 tablespoons will be collected at each blood draw). The risks of drawing blood include some discomfort from the needle in your arm, bruising, swelling at the needle site and, in rare instances, infection or fainting.

You will also be informed of any new significant side effects that develop during the course of this research study, or others regarding the use of demcizumab.

Radiation exposure:

- Risk relevant to the radiation exposure due to the following procedures: Radiographic evaluation: Conventional CT, Spiral CT, or MRI of the chest, abdomen, and pelvis performed in screening, the same radiographic technique of each region must be used consistently throughout the study. Radiographic evaluation: Conventional CT, Spiral CT, or MRI of the head performed in screening

PREGNANCY

Pregnancy Risk with study treatments

There is a very high risk that demcizumab may be harmful to an unborn baby (embryo or fetus) or newborn child. In addition, Abraxane® and gemcitabine can cause harm to an unborn child if given to a pregnant woman. You cannot take part in this study if you are pregnant or breast-feeding. Because of the possible risks to an unborn child, if you are a female who can become pregnant, you will be asked to take a pregnancy test prior to starting study treatment. It is important that both men and women take steps to prevent pregnancy through the use of adequate contraception (for example, a barrier or hormone method or abstinence) prior to study entry during the study and for 6 months after completion of the study.

Females: If you decide to take part in this study, you should avoid becoming pregnant while receiving the study treatment. You must commit to complete abstinence from heterosexual contact, or agree to use medical doctor-approved contraception throughout the study and for 6 months following completion of the study without interruption. If you become pregnant while on the study or within 6 months following completion of the study, you must tell the study doctor right away. If this happens while you are on the study, the study treatment will be discontinued. The study doctor will follow you and your pregnancy to completion.

Males: If you have a partner of childbearing potential, you should avoid fathering a child while receiving study treatment and for 6 months after completion of the study. You must agree to complete abstinence from heterosexual contact or use a condom during sexual contact with a

female of child bearing potential while receiving study treatment and within 6 months after completion of the study. If your partner becomes pregnant while you are receiving study treatment or within 6 months after completion of the study, you must tell the study doctor right away. If your partner becomes pregnant while you are on study, you will remain on the study. If your partner becomes pregnant during the study or within 6 months after completion of the study, you and/or your partner will be followed through the first well-baby visit or longer if any abnormality is present.

POTENTIAL BENEFITS

There is no guarantee that there will be any direct benefit to you if you take part in this research study. The treatments you receive may be harmful. It is possible that the information learned from this study may be helpful in the future to other people with cancer.

SIGNIFICANT NEW FINDINGS

Any significant new findings regarding demcizumab that become known during the course of this research study that might reasonably affect your willingness to participate in this study, will be provided to you in a timely manner.

ALTERNATIVE TREATMENTS AND PROCEDURES

If you decide not to participate in this study, you will continue to receive medical care to which you were entitled prior to your participation in this study. Your doctor will discuss other options available to you. Your choice not to participate in this study will not affect your medical care in any way.

TERMINATION OF PATIENT PARTICIPATION

Your participation in this research study may be terminated at any time for medical reasons or because the sponsor finds it necessary to limit or terminate this clinical trial. Some reasons for termination include progression of your disease, any other illness that prevents further administration of demcizumab, unacceptable adverse events, or BNP and/or LVEF values, general or specific changes in your condition that make further treatment unacceptable in the opinion of your doctor, and protocol non-compliance.

Your doctor may decide to hold or stop the demcizumab or placebo injections at any time during the study for safety reasons.

If your doctor or the sponsor decides to withdraw you from the study, you will undergo the same assessments listed under Termination Visit. In addition, your doctor will discuss with you alternate therapies for your disease.

COSTS AND COMPENSATION

The cost of all "standard of care" assessments related to your participation in this study and your medical care will be billed to you and/or your insurance company. These are tests that would normally be performed in subjects to evaluate their cancer. Due to the investigational nature of this research study, insurance companies or government health care programs may limit their obligation to pay for experimental treatments and their consequences. You may want to discuss this with your insurance company before agreeing to participate. The cost of all non-standard of care assessments will be paid for by OncoMed.

You will not be paid for participation in this study.

COMPENSATION FOR RESEARCH-RELATED INJURY

If you are physically injured as a direct result of demcizumab or a study procedure properly performed under the plan for this study and it is not due to a pre-existing medical condition or underlying disease, or your failure to follow the instructions provided by your doctor or another member of the study team, OncoMed will reimburse you for the reasonable medical expenses for medically necessary treatment of that injury which are not covered by another payor, your own insurance or health care program. No other compensation is available from OncoMed if any injury occurs.

CONFIDENTIALITY

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 Website will include a summary of the results. You can search this website at anytime.

HOW WILL YOUR CONFIDENTIALITY BE RESPECTED AND THE PRIVACY OF YOUR PERSONAL INFORMATION MAINTAINED?

You have the right to control the use and disclosure of your personal information. Basic personal information will be recorded including your name, contact details, gender, height, weight and racial origin (to be used only for clinical purposes), as well as information on your medical history, and clinical data collected about your participation in the study. All this information will be used for research and clinical purposes only, including without limitation the pharmacokinetic and optional DNA research described in this consent form.

The following people may also access these records: representatives of the FDA, other regulatory authorities, the Institutional Review Board/Independent Ethics Committee, OncoMed representatives and monitors, and OncoMed collaborators and licensees

All personnel accessing your records are required to respect your confidentiality at all times.

To ensure privacy, your name and other identifying information will not be attached to records or samples released for research purposes. Instead, you will only be identified by a code. Only the study doctor and authorized personnel will be able to connect this code to your name, by a list that will be kept securely by the study site for 2 years after marketing application approval. If no application is filed, these records must be kept for 2 years after the study is discontinued and the applicable regulatory authorities are notified. Your date of birthmay also be recorded to help identify your study record. Your coded data will be forwarded to OncoMed and its service providers for activities related to the study e.g. laboratory analysis. It will be transferred into a computer database and processed to allow the results of this study to be analyzed and reported or published. If the results of the study are published, your identity will remain confidential, you will not be identified by name, picture, or by any other personally identifying information.. A list of companies to whom your coded information is transferred is available from OncoMed via your study doctor.

EMEA: Under data protection law [identification of national law] your study site and OncoMed Pharmaceuticals shall be jointly responsible as ‘controllers’ for ensuring that your information is safeguarded. OncoMed has appointed [PPD local company name] as its ‘representative’ in your country to fulfill its obligations under this law.

The information that we collect from you may be transferred to, and stored at, a destination outside the European Economic Area ("EEA"). It may also be processed by staff operating outside the EEA who work for us or for our representative. By participating in the research study, you agree to this transfer, storing or processing outside of the EEA. When transferring such information to countries outside of the EEA, that do not have the same protections as your country we will make sure that your information will be treated with a goodlevel of protection as required under your local data protection laws.

APAC: Under data protection law [identification of national law] your study site shall be responsible for ensuring that your named personal information is safeguarded

USA: Because of the research goals of this study, however, your study records cannot be kept completely confidential. The sponsor of this study is OncoMed Pharmaceuticals.

The study data may be transferred to other countries for processing, including countries not covered by data protection legislation similar in scope to the data protection legislation of your country, or at all. The laws of your state may provide further protection.

CANADA: Under federal data protection law, The Personal Information Protection and Electronic Documents Act (PIPEDA) and regional specific regulations, your study site shall be responsible for ensuring that your information is safeguarded

You have the right to access, through your study doctor, all the information collected about you and, if applicable, ask for corrections. But, in order to protect the scientific integrity of the study, the treatment you received in this study needs to remain unknown (i.e., blinded) until the study data is analyzed. Recipients of your information may be in countries that do not have data protection safeguards and rights. In such case, OncoMed and its authorized representatives, and regulatory authorities, shall anyway seek to maintain confidentiality within the limits of local laws in these countries and comply with the data export requirements of your country, including any requirements to ensure an adequate level of protection.

If you should withdraw from the study, data collected prior to your withdrawal may still be processed along with other data collected as part of the study. Normally no new information will be collected for the study database unless you specifically consent to such collection. However, the law does require that any side effects you may suffer are documented and reported. To complete the study findings, your long term health status may also be recorded (unless you object).). Following the end of the study, or after you have withdrawn from the study before its conclusion, your study doctor (or appointed delegate) may seek to establish your long term health status by accessing your hospital records, or publicly available sources such as national registries, newspaper obituaries and social networking websites. Attempts may also be made to contact you or your relatives to ascertain this information. If you do not want this information about you to be collected, you may record your objection with your study doctor at any time.You have the right to require that any previously retained samples are destroyed.

WHAT WILL HAPPEN TO YOUR DATA?

This clinical study may only be performed by collecting and using your medical information. Data protection laws give you the right to control the use of your personal information. Therefore, by signing this form you specifically authorize your information to be checked, transferred and processed as follows:

- The authorized representatives of OncoMed, the Ethics Committee and regulatory authorities' inspectors may review your medical information by direct access to your medical records.
- Study data, including your coded medical information, may be used and shared for legitimate study and scientific purposes, including if you do not object, for future use in medical or pharmaceutical research.

☐ I agree to the use of my coded medical information for future research purposes.

Signature: _____

☐ I don´t agree to the use of my coded medical information for future research purposes.

Signature: _____

- Study data may be transferred to other countries for processing, including countries not covered by data protection legislation similar in scope to the data protection legislation of your country, or at all.

HAS THE STUDY RECEIVED MEDICAL OR ETHICAL APPROVAL?

The Ethics Committee has given this study a positive opinion.

You will be asked to review and sign a HIPAA (Health Insurance Portability and Accountability Act) Research Authorization Form requesting your authorization to collect, use, and disclose your medical information.

OR IF SITE DOES NOT HAVE OWN HIPAA FORM:

AUTHORIZATION TO USE AND DISCLOSE MY HEALTH INFORMATION

I authorize (give permission to) insert name of study site to use and disclose (share) my health information solely for the purposes of this research study and research directly related to the use of demcizumab. I understand that my health information that I am authorizing to be used and disclosed (Authorized Health Information) includes all health information about me that has been and will be created or received by (SITE) and that is in my medical records maintained by (SITE).

I understand that I am free at any time to restrict the (SITE's) use and disclosure of my Authorized Health Information, without penalty or other consequences. However, I also

understand that I may be denied participation in, or continued participation in, this research study if at any time I choose to restrict the (SITE's) use and disclosure of Authorized Health Information that is necessary for the completion of this research study.

AUTHORIZED PERSONS AND RECIPIENTS

I authorize the following person(s) and groups of persons to request, receive, and use my Authorized Health Information: representatives of the FDA, other regulatory authorities, the Institutional Review Board/Independent Ethics Committee, OncoMed representatives and monitors, and OncoMed collaborators and licensees. I authorize (SITE) to disclose my Authorized Health Information to these persons and groups of persons.

RE-DISCLOSURES TO THIRD PARTIES

I understand that once (SITE) discloses my Authorized Health Information to the recipient(s) identified in the previous section Authorized Persons and Recipients, (SITE) cannot guarantee that the recipient(s) will not re-disclose my Authorized Health Information to other persons who may not be bound by this informed consent form.

EXPIRATION DATE

My authorization (permission) to use and disclose my Authorized Health Information will continue indefinitely, but that use and sharing will only be for the purposes described in this informed consent form.

EFFECT OF MY REVOCATION OF AUTHORIZATION TO USE AND DISCLOSE AUTHORIZED HEALTH INFORMATION

I understand that my authorization for (SITE) to use and disclose my Authorized Health Information will remain in effect until I withdraw my permission by sending my written notice of revocation (withdrawal of permission) to the Privacy Office listed in the Questions section. My written revocation will be effective immediately upon (SITE's) receipt of my written notice, except that the revocation will not have any effect on any actions take*n* by (SITE) in relying on this authorization before it received my written notice of withdrawal of permission.

QUESTIONS

If you have any question about the study and/or its procedure or safety, you may contact Dr. (Name of Investigator) at (telephone number). In the event of any injury, you may contact Dr. (name) at (telephone number). You may also call (Name) at (telephone number) for information on experimental patients' rights.

If at any time during this research study you feel that you have not been adequately informed of your rights with respect to the privacy of your health information, or you feel that the privacy of your health information has not been adequately protected, you may contact or visit (Site's)

privacy office during normal working hours at (Privacy Office name) at (telephone number and address).

VOLUNTARY PARTICIPATION AND DOCUMENTATION OF CONSENT

Your decision to participate in this study is entirely voluntary. You may refuse to participate in or withdraw from the study at any time without prejudice or loss of benefits to which you are otherwise entitled. A signed copy of this consent form will be given to you for your records and a copy will be retained by the investigator for his or her files

By signing the form below, you acknowledge that you have read the above information about this research study, and have had a chance to ask questions to help you understand your participation in this study and how your information will be used.

_____ _____

Signature of Subject or Subject's Authorized Representative **Date**

_____

Printed Name of Person Obtaining Informed Consent

_____ _____

Signature of Person Obtaining Informed Consent **Date**

_____

Printed Name of Witness*

_____ _____ _____

Signature of Witness* **Date**

*If the Principal Investigator or Institutional Review Board deems a witness signature is necessary.

APPENDIX G: SAMPLE PHARMACOGENOMICS AND TUMOR DNA TESTING INFORMED CONSENT

WHAT IS THE PURPOSE OF THIS PART OF THE STUDY?

The cells of your body contain deoxyribonucleic acid, or DNA for short. DNA is passed down from your parents. Genes carry the DNA that determine your physical appearance such as the color of your eyes and hair. Differences in our genes help explain why we all look different. Differences in our genes may also help explain why some drugs work and are safe in some people, but not in others. Differences in our genes also help explain why some people get certain diseases, but others do not.

The sponsor would like to study the differences in people's DNA to learn more about diseases and response to drugs. This information will be used to try to develop safer and better drugs. To do this, the Sponsor would like to do DNA tests related to OMP-21M18 and the diseases for which this drug is developed. The DNA tests are only for research. The tests are not for your medical care. All volunteers taking part in the main study are also being invited to take part in DNA research (where possible).

WHAT AM I BEING ASKED TO DO?

You are being asked to give one small blood sample (10 mL, about 2 teaspoons) at Study Day 0. Blood will be drawn from a vein using a needle. DNA will be extracted from your blood sample. Your DNA may be tested for specific genes relevant to OMP-21M18 (the study drug), the Notch/DLL4 pathways (the targets of the OMP-21M18) and/or other genes related to your cancer. Only DNA research related to OMP-21M18 or to the diseases for which this drug is developed will be performed. No blood sample for DNA research will be taken from you unless you sign and date this Informed Consent Form.

In addition, if a piece of your tumor was previously collected as part of your diagnosis, you are being asked to have DNA testing performed on your tumor. DNA will be extracted to help to identify biomarkers that could be used in the future to predict which patients are more likely to respond to OMP-21M18 and gemcitabine treatment. Analysis of candidate genes and/or proteins relevant to the Notch pathway may be performed (e.g., Notch1, Hey L, FBW7, etc.). No DNA research will be performed on your tumor unless you sign and date this Informed Consent Form.

The Sponsor will store the samples until there is no DNA left.

You can also decide not to take part at all in DNA research. Your decision to give, or not to give, a DNA sample will not affect the medical care that you receive from your study doctor or his/her staff. Your participation is voluntary.

HOW WILL MY IDENTITY AND RESULTS BE KEPT CONFIDENTIAL?

The Sponsor has taken several steps to keep your identity and results confidential. These are described below.

a) Coding of your DNA Sample

Your DNA sample will not have your name or address on it. Your DNA sample will be coded with your Subject number from the main study. After the study is officially over, the Subject number will be removed from your DNA sample. Your DNA sample and results will be labeled with a new number.

b) Restricted Access to Your DNA Sample

The Sponsor will control your DNA sample. Your DNA sample will be stored in a secure room at a facility in Redwood City, CA, or other site designated by the sponsor. Only authorized staff are allowed to enter the room. Your DNA sample may be transferred to other research partners working with the Sponsor. DNA samples transferred to research partners will not contain your Subject number. Your DNA sample will not be sold, loaned, or given to any other independent groups for their own use. Research partners working with the Sponsor are not allowed to share DNA samples with anyone else.

c) Restricted Access to Results

Your DNA results will be stored by the Sponsor both on paper and in computer records. You will not be identified by name in these records. Your results will only be labeled with a code number. This is to protect your privacy. Your results will be kept as long as necessary. The following people may see your test results:

- The Sponsor
- Research partners working with the Sponsor
- Independent Ethics Committees/Institutional Review Boards
- Regulatory authorities, like the Food and Drug Administration (FDA) or the European Medicines Evaluation Agency (EMEA)

Unless the law requires it, your individual results will not be given to anyone who is not listed above. For example, your results will not be given to employers, insurance companies or family members. Research partners working with the Sponsor may not use or share your results without permission from the Sponsor.

DNA results from the study may be published or added to public databases. They also may be presented in public meetings. No publication or presentation will identify you by your code number or name.

d) Separate Storage of DNA Forms

Your study doctor will keep your signed DNA informed consent form, and any other DNA forms, separate from your other medical files. People who have access to your medical files (such as insurance companies) would not know that you took part in a DNA research study by looking at your medical files. You will be given a copy of your signed DNA consent form.

WHAT IF I CHANGE MY MIND LATER?

If you change your mind and decide later that you no longer want to take part in DNA research, you may ask for your DNA sample to be destroyed as long as the study is not officially over. You can stay in the main study even if you change your mind about taking part in DNA research.

WILL I GET MY DNA TEST RESULTS?

The tests will be performed in a research laboratory. Results from a research laboratory may not always be exact. They cannot be used to make a diagnosis about your health. Also, research laboratories cannot give advice on health or health risks. For these reasons, the results of your DNA tests will not be given to you or your study doctor (or his/her staff).

WHAT ARE THE BENEFITS?

You will not directly benefit from taking part in this DNA research. This research could provide information about OMP-21M18 or the diseases for which this drug is developed. This information could help others in the future.

WHAT ARE THE RISKS?

There may be some pain or bruising from the needle stick used to draw the blood. Some people may faint when their blood is drawn. Very rarely, there may be an infection at the place where the needle went into the skin. Any problem that you have from drawing blood will be handled the same way as in the main study. Your research results cannot be used to make a diagnosis about your health.

WILL I BE PAID FOR TAKING PART OR FOR THE USE OF MY RESULTS?

You will not be paid for taking part in the DNA research part of the study. You will not be paid for any use of your DNA sample or results or for any inventions that are made from them. If you take part, you are providing your DNA sample for use by the Sponsor. The Sponsor intends to own any use of the results, treatments, or inventions that can be made from the research.

QUESTIONS

If you have any question about the study and/or its procedure or safety, you may contact Dr. (Name of Investigator) at (telephone number). In the event of any injury, you may contact Dr. (name) at (telephone number). You may also call (Name) at (telephone number) for information on experimental subjects' rights.

If at any time during this research study you feel that you have not been adequately informed of your rights with respect to the privacy of your health information, or you feel that the privacy of your health information has not been adequately protected, you may contact or visit (Site's) privacy office during normal working hours at (Privacy Office name) at (telephone number and address).

VOLUNTARY PARTICIPATION AND DOCUMENTATION OF CONSENT

Your decision to participate in this part of the study is entirely voluntary and. you may choose not to participate in this part of the study without prejudice or loss of benefits to which you are otherwise entitled in the remainder of the study. A signed copy of this consent form will be given to you for your records and a copy will be retained by the investigator for his or her files.

By signing the form below, you acknowledge that you have read the above information about this research study, and have had a chance to ask questions to help you understand your participation in this study and how your information will be used.

I consent to the provide the Optional Pharmacogenomics Specimen

☐ **Yes** ☐ **No**

I consent to allow my tumor specimen to be analyzed for DNA

☐ **Yes** ☐ **No**

_____
Printed Name of Subject or Subject's Authorized Representative

_____ _____
Signature of Subject or Subject's Authorized Representative **Date**

_____
Printed Name of Person Obtaining Informed Consent

_____ _____
Signature of Person Obtaining Informed Consent **Date**

_____
Printed Name of Witness*

_____ _____
Signature of Witness* **Date**

*If the Principal Investigator or Ethics Committee deems a witness signature is necessary.