INFORMED CONSENT DOCUMENT – Pilot Phase

Project Title: **A therapeutic trial for safety and preliminary efficacy of the combination of axitinib and selenomethionine (SLM) for adult patients with advanced metastatic clear cell renal cell carcinoma (CCRCC)-Pilot**

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This consent form describes the research study to help you decide if you want to participate. This form 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 as a research subject.

- If you have any questions about or do not understand something in this form, you should ask the research team for more information.
- You should discuss your participation with anyone you choose such as family or friends.
- 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.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We are inviting you to participate in this research study, because you have been diagnosed with advanced metastatic clear cell renal cell carcinoma (CCRCC), stage IV and have previously been treated.

The purpose of this research study is to test the safety of combining two oral drugs, selenomethionine (SLM) and axitinib and see what effect (good or bad) it has on people who have CCRCC. We want to find out what dose of selenomethionine (SLM) is appropriate, causing as minimal side effects as possible and see if the combination of the two drugs improves the response rate in people with CCRCC.

This was intended to be a two-part study, also known as two phases. We have finished the escalation phase of the study. That portion of the study looked at finding the maximum tolerated dose (MTD) of study drug, selenomethionine (SLM). The second part of the study, expansion phase, is now ongoing, where subjects are receiving the study dose determined by the escalation phase.

During the escalation portion of the study, we noticed that people with a lower BSA, (Body Surface Area or "body size") had higher concentrations of the study drug in their blood, than subjects who had a higher BSA. We think this difference in blood concentration across people with different BSA might impact how well the drug works, so we are conducting this "pilot" phase as a third part of the overall study, to examine dose-concentration relationship and to determine what dose of selenium is needed based on BSA to achieve the blood concentration range that we are looking for.

We are asking you to participate in the pilot phase of this study where we look more closely at how BSA effects blood levels of SLM. In this phase, your dose will be between 4000 and 6000 mcg of SLM, depending on your BSA. SLM will be taken by mouth twice a day for 14 days. On day 14 we will check

the levels of SLM in your blood. Starting on day 15, you will take SLM only once a day in combination with axitinib by mouth twice a day. Your treatment will continue until your disease progresses or you have unacceptable side effects.

Selenium (Se) is a natural element present in the earth's crust often in association with sulfur-containing compounds. Humans get their dietary requirements mainly from food. Selenium compounds have been used in various clinical trials, mainly in chemoprevention. In this study Selenium will be administered in the chemical composition of selenomethionine (SLM). SLM is not approved by the FDA for the treatment of metastatic clear cell renal cell carcinoma.

Axitinib is a tyrosine kinase inhibitor approved by the FDA for the treatment of subjects with advanced renal cell carcinoma. Subjects with other types of cancer have also received treatment with axitinib and other cancer types have responded to axitinib treatment.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 65 people will take part in all phases of this study. We have already enrolled 16 people in the Escalation phase of the study. We would like to enroll 10 people in this pilot phase, and the rest of the subjects we enroll will be in the Expansion phase. This study will be conducted by investigators at the University of Iowa.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement could last indefinitely. This study consists of treatment "cycles" and each cycle is 28 days long. You will continuously repeat the cycles, until you experience disease progression, or unacceptable side-effects. Once you complete all cycles of the study, you will have an End of Treatment visit approximately 28 days after your last dose of study drug.

Visits will range from 1 to 4 hours in length. We may also call you on the telephone periodically to see how you are doing. If your disease progresses, we will continue to see you and offer follow-up care outside the research study.

WHAT WILL HAPPEN DURING THIS STUDY?

If you are eligible and choose to take part in this study, you will receive SLM and axitinib. You will receive both drugs by mouth. The dosages may be adjusted should the study doctor decide that you are having difficulty handling the initial dose.

Before you begin the study:

You will need to have the following procedures to find out if you can be in the study. Many of these procedures are part of your regular cancer care and would be done even if you do not join the study.

- Demographic information collected (age, gender, etc.)
- Medical history (including history of previous, present and related conditions and treatment)
- Physical examination (complete physical examination, including height, weight)
- Vital signs (including blood pressure, heart rate, respiratory rate, after 5 minutes supine rest and body temperature)
- Assessment of ECOG performance status
- Blood samples will be drawn, to study kidney function, liver function, thyroid function, white cells, red cells, and platelets, and glucose. These would be standard tests. Additionally, samples will be

used to study the SLM concentration in your blood and blood for additional storage. In total, approximately 3-4 teaspoons will be drawn at the visits.

- Urinalysis (dipstick tests)
- Assessment of cardiac risk factors (Lipid profile, smoking, family history of cardiac disease, use of aspirin)
- You will have tumor imaging to locate and measure the cancer in your body
- Current medications recorded
- 12-Lead ECG after 5 minutes supine rest.
- Pregnancy test (this test is mandatory in women of child-bearing potential). Results of the pregnancy test must be negative for you to participate in this study.
- Archival Tumor Sample. You are being asked to have a sample of your tumor tissue which was collected **before** you started the study (this is called an Archival Tumor Sample), to be stored and tested for research testing. Your study doctor or study staff will request the archival tumor tissue sample from the medical facility where it was originally obtained and arrange for analyses of additional biomarker tests. You do not have to agree to the tissue submission. If you say no, you can still participate in the study. **You will be asked to indicate your willingness to submit archival tumor tissue at the end of this consent document.**

Many of the tests listed above will be repeated during the study. For a better understanding of when these tests are done, please refer to the following table.

Study Treatments

The study team will help you understand what is expected for you in terms of scheduling your visits.

	Screening	SLM Run-in Phase		Cycle 1				Cycle 2 and on				End of Treatment	Follow-up (every 6 months)
		Week 1	Week 2	Week 1	Week 2	Week 3*	Week 4	Week 1	Week 2	Week 3*	Week 4		
Medical History	X			X									
Current medication	X			X		X		X		X			
Physical exam & Vitals	X			X		X		X		X		X	
Performance status evaluation	X			X		X		X		X		X	
ECG	X												
Blood Samples	X	X	Day 14	X		X		X		X		X	
Urinalysis (dipstick)	X			X				X				X	
Pregnancy test for women of childbearing potential	X			X				X					
miRNA (blood draw)		Day 1	Day 14										
Fresh Tissue biopsy (for up to 20 patients in pilot/expansion phase)		Day 1	Day 14 (+/- 3 days)	8 weeks after first dose of SLM plus Axitinib (Cycle 3) (+/- 3 days)								X	
Archival tumor tissue	X												
SLM Concentration & Additional blood for storage		X	X					X					
CT +/- Bone scan	X (within 28 days from consent)			These scans will begin at Cycle 5, day 1 and repeated every 8 weeks +/- 5 days, as clinically indicated. If you are not having symptoms, scans may be done every 4 months.									
Dual Energy CT	X		Day 14 (+/- 2 days)	8 weeks after first dose of SLM plus Axitinib (Cycle 3)									
SLM Dosing		→	→	→	→	→	→	→	→	→	→		
Axitinib Dosing				→	→	→	→	→	→	→	→		
Adverse Event Assessment		→	→	→	→	→	→	→	→	→	→	→	
Safety Phone Call			X		X								X

*If necessary due to COVID 19 precautions, week 3 visits may be replaced with a telehealth visit and blood samples obtained al local clinic

You will be asked to complete a study dosing diary while you are taking the study medication. It will be given to you at the start of the study. We ask you to bring your dosing diary and study drug back to the clinic at each visit so the study staff can make sure you are taking your medication correctly. The study staff will review the dosing diary with you to ensure accuracy and assess how often you were able to take your medicine.

During the course of the study, if you participated in or participate in the future in GU-MER IRB#201304826, we will obtain research tissue and corresponding data from you obtained through the GU-MER IRB#201304826. This is different than archival tissue as the GU-MER tissue is considered "research tissue."

Tumor Imaging (DUAL-Energy CT scan and CT scans)
During this study, you will have tumor imaging. At three time points Screening, Day 14, and Cycle 3, you will have a Dual-Energy CT scans. A Dual-Energy CT scan is similar to a regular CT scan, but provides us with a little more information. The Dual-Energy CT scans performed are considered research only and will be paid for by the study. At all other time points, you will have a standard CT scan. The following will also occur prior to and during the Dual-Energy CT scans:

Catheter Placement and Blood Draw:
An IV catheter will be placed in your right arm by a Holden Comprehensive Cancer Center (HCCC) nurse or a study nurse coordinator. The catheter will be used during the Dual Energy CT scanning procedures to deliver contrast agent or dye. Blood samples will also be drawn from the IV catheter to check your serum creatinine level (this test tells us how well your kidneys are functioning—if this level is abnormal, you will not be able to participate in the study). If you are a female of childbearing potential, you will have a urine pregnancy test on this return visit as well. The IV catheter will be kept in your arm for the duration of the study visit and will be used to deliver the contrast during the CT scan.

<u>CT Scans:</u>
You will then be taken to our CT Imaging Suite. Once there, the CT technologist will answer any questions you may have. If you have any metallic items on your body between your nose and abdomen (jewelry, zippers, piercings that can be easily removed, etc.) you will need to remove them prior to being put in the scanner. If you need to remove an article of clothing, you may use the private restroom in the CT Imaging Suite. Then you will be positioned on the moveable exam table of the CT scanner. We will connect you to an EKG machine (which will monitor your heart rate throughout the scans), a pulse oximeter (which is a small finger clip that has a sensor to monitor the amount of oxygen in your blood) and a blood pressure cuff. We will then move on to the scanning procedures:

For each visit a series of CT scans will be taken of your chest and you will be asked to hold your breath for about 5-8 seconds while the CT scans are taken.

- The first type of scans that will be done are called *Topograms.* These are a type of scout scans, which are similar to an x-ray, and help the CT technologist make sure that you are positioned correctly in the scanner. These are not counted as one of your CT scans. You will be instructed to breathe normally and we will then tell you to take in as deep of a breath as you can and hold it while an image is being taken of your lungs. Once again, we will ask you to return to normal breathing for a few minutes.
- The *dual energy CT scan*: For these scans, a contrast agent (dye) will be injected through the IV catheter in your arm while the x-rays are taken. The injection of the contrast agent during the CT

scanning allows us to see where and how blood distributes in your lungs. We will start the contrast injection and then ask you to take in a deep breath in and hold then have you hold your breath. The CT scanner is set to begin scanning your lungs after a certain amount of contrast has gone in. Once the scan is done, we will have you return to normal breathing.

Tumor Biopsy

Up to 20 patients in the Expansion Part 2 and the pilot phase will have up to up to four tumor biopsies. The biopsies will occur before the start of selenomethionine (SLM), at Day 14, Cycle 3, at the time of progression. The biopsies are being done to examine the effect of SLM on your tumor.

A biopsy is the removal of a sample of tissue taken from your disease site. The biopsy may be taken by a small needle. The tissue taken from the biopsy can also be used to perform additional biomarker tests. The principal investigator and/or treating physician/staff will discuss the details regarding your biopsies before they occur. The biopsy patients will be chosen by the treating oncologist, with assistance with imaging techniques. If 20 patients have already had biopsies, you may not be eligible for the biopsy and in that case, they will not occur. Dr. Zakharia will let you know if this occurs.

Blood Storage for Future Use

All patients will have a blood drawn before the start of selenomethionine (SLM) and repeated on day 14 after starting treatment. This blood will be stored and might be used later to study proteins in your blood. The blood draw must happen before starting SLM and 2 hours after on Day 1. Blood will also be drawn two hours after taking the SLM dose at Cycles 2, 3, 4 and 7, then at Cycles 10 and 13.

The tests we might want to use to study your blood samples may not even exist at this time. Therefore, we are asking for your permission to store your blood samples so that we can study them in the future. These future studies may provide additional information that will be helpful in understanding CCRCC, but it is unlikely that what we learn from these studies will have a direct benefit to you. It is possible that your blood samples might be used to develop products or tests that could be patented and licensed. There are no plans to provide financial compensation to you should this occur.

If you agree now to future use of your blood samples but decide in the future that you would like to have it removed from future research, you should contact Yousef Zakharia, MD at 319-384-8076. However, if some research with your blood samples has already been completed, the information from that research may still be used.

Follow-Up:

You will be followed as long as we are able to maintain contact with you. This follow-up will be completed over the telephone. If you are not reachable over the telephone, we will utilize publicly available records to update your living status at least every 6 months.

General Reminder: Please inform your study doctor before you start any prescription drug or other medication (including over-the-counter drugs and herbal supplements) not prescribed by the study doctor.

It is possible the timing of your in-person study visits may happen every other month, rather than every month. This will only happen if study doctors think this schedule will be safe for you, and if you live very far from the study site.

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. Selenomethionine (SLM) has only been studied in a small number of subjects. While in this study, you may develop any of the side effects listed below.

In addition, there may be side effects that are currently unknown, or that we cannot predict. You will be monitored for side effects throughout this study. Your condition may not get better or may become worse during this study.

Selenomethionine (SLM):

The following list of side effects occurred in a study giving a Selenium compound much like selenomethionine (SLM) at much higher doses than what will be given in this study. Two patients withdrew from the study due to unacceptable toxicities. The side effects listed below occurred in 10% to 45% of the 20 patients who participated.

- Constipation
- Diarrhea
- Nausea
- Retching (gagging)
- Vomiting
- Fatigue
- Decreased appetite
- Arthralgia (joint pain)
- Muscle spasms
- Myalgia (pain in muscles)
- Dizziness
- Headache
- Hypoaesthesia (numbness)
- Lethargy (tiredness)
- Alopecia (hair loss)
- Nail disorders consisting of redness and blister formation or brittle nails with white spots
- Skin pain

In another study a selenium compound was given orally to 20 patients with intermediate and high-grade non-Hodgkin lymphoma at a dose of 200µg/kg/day on days 3 to 7 following their first course of CHOP chemotherapy. This equates to a dose of 14,000µg daily. It was reported that 90% of patients experienced garlicky breath odor and some gastrointestinal upset.

Side effects also included:

- Mild fever
- Vomiting
- Anorexia
- diarrhea
- Garlicky breath odor

- Itching
- Numbness
- Elevated liver function tests.

Axitinib:
The most common side effects of axitinib (occurring in more than 20% of patients) include:

- diarrhea
- high blood pressure
- fatigue
- decreased appetite
- nausea
- voice changes
- pain
- swelling or blisters on your hands and feet
- weight loss
- vomiting
- constipation
- hypothyroidism
- protein in your urine (proteinuria)

Other side effects of axitinib (occurring 10-20% of patients) include:

- Cough
- Headache
- Shortness of Breath
- Joint pain
- Abdominal pain, including pain or discomfort in upper abdomen
- Back pain
- Inflammation of the mouth and lips
- Pain in extremity
- Rash
- Weakness or low energy
- Mucosal inflammation
- Dizziness
- Change in taste
- Blood and liver test abnormalities

Other rare but significant side effects have occurred, including a severe increase in blood pressure that caused a stroke, severe bleeding, blood clots in a vein, blood clots in the heart, brain injury (reversible posterior leukoencephalopathy syndrome) that caused headache, confusion, seizure and vision loss, decreased thyroid gland function requiring medication, decreased liver function, decreased kidney function, and the development of holes in the intestine.

If you develop one or more of these side effects, your study doctor may decide to reduce your axitinib dose. Your study doctor may offer you treatment for your side effects to lessen the severity. If your

side effects are severe enough, your study doctor may decide to permanently discontinue your participation in this study.

Other Procedure Risks:

Tumor Imaging (CT and Dual-Energy CT scans)
Some CT scans require you to take a "contrast solution" injected into a vein. It is possible that the contrast solution may cause you to have nausea, vomiting, itching, or skin rash. In rare cases, it may cause your throat to swell and make it hard to breathe. These may be signs of an allergic reaction so tell the study doctor right away if you have any of these side effects. You may have some discomfort from lying still in an enclosed space for a prolonged period of time.

RADIATION RISKS
The maximum amount of radiation from the research related radiation procedures for this study is equivalent to approximately 130% of the annual radiation limit for a medical worker. Although there are no proven harmful effects from this amount of radiation, long term effects on your health such as cancer cannot be ruled out with certainty. This dose estimate takes into account only the exposure to research procedures in this project. If you have participated in other research studies involving radiation exposure, you should be aware that the risk of effects of radiation exposure is thought to add up across all your exposures (including studies performed as part of your medical care).

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 each exposure 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.

Blood Testing:
The following side effects could occur from blood testing that will be done as part of this study:

- Pain, tenderness or bruising may occur at the spot where the needle is inserted.
- You may faint.
- Rarely, infection may occur at the spot where the needle is inserted.

Biopsy:
Serious problems from a biopsy are not common. Side effects may include bleeding or infection of skin at the biopsy site. People with bleeding problems have a higher chance for this. If you have bleeding problems, pressure will be put on the biopsy site to stop the bleeding. In rare cases, you may be given a blood product (clotting factor or platelets) in a vein in your arm before the biopsy to prevent bleeding after the biopsy.

Risks to Reproduction, Unborn Babies and Nursing Infants:
General Statement
You must not be pregnant or breastfeeding, and you should not become pregnant or breastfeed while you are taking the study drug. You must use an adequate method(s) to avoid pregnancy for the duration of this study. If you are a man who is sexually active with a woman of childbearing potential, you should also use an adequate method(s) of birth control to avoid pregnancy of your partner for the duration of this study. You should immediately contact your study doctor if there is a change in your

method(s) to avoid pregnancy.

Unforeseeable Risks
There may be unknown risks to you, your unborn baby or nursing infant if you are or become pregnant during this study or are breastfeeding during this study.

Use of a Study-Prohibited Contraceptive Method
Your study doctor will discuss acceptable birth control methods for use during your participation in this study. Any birth control method used should be discussed with your doctor if it is started during the course of the study.

Occurrence of Pregnancy or Suspected Pregnancy
If you become pregnant, suspect pregnancy or if you missed your period or it is late, or if you have a change in your usual menstrual cycle (e.g., heavier bleeding during your period or bleeding between periods), you should immediately contact your study doctor.

Discontinuation from the Study
Should you become pregnant during this study, you will immediately have the study medication permanently discontinued and be referred for obstetric care; unless, after further discussion between your physician and the Sponsor of this research, it is decided that the benefit of continuing therapy would outweigh the risk for stopping therapy.

You will continue to be followed for any side effects or potential benefits of the study treatment. Your doctor will discuss this with you, as well as options for additional appropriate care for your cancer.

WHAT ARE THE BENEFITS OF THIS STUDY?

We don't know if you will benefit from being in this study.

However, we hope that, in the future, other people might benefit from this study because of the knowledge gained about the treatment of Clear Cell Renal Cell Carcinoma.

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 have the option of other chemotherapy treatment or other investigational programs. You also have the option of receiving no treatment for your cancer. Please talk to your doctor about these other options.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You may have costs for being in this research study. Sabinsa Corporation located in NJ, USA, will provide SLM free of charge. Axitinib is being provided free of charge by Pfizer. The optional tumor biopsies, Dual Energy CT scans performed and some of the blood tests will be provided free of charge for this study. This study is being funded by Pfizer, and a grant from the PACT Committee through the

Holden Comprehensive Cancer Center. Any medications, tests or procedures that are part of your regular medical care will be billed to you/your health insurance company.

If your health insurance company or Medicare requires any co-payment, co-insurance or deductible, you

will be responsible for making that payment. Sabinsa Corporation, Pfizer and the PACT grant will not pay for other treatments or tests considered part of the standard of care for your disease. Your insurance company may not pay for medications or procedures used for your regular medical care if you are in a research study. Some examples of standard procedures include routine laboratory blood tests, physical examinations, x-rays, CT scans performed at screening and during cycles, MRIs, surgeries, blood transfusions, physicians' charges and routine medical care. Examples of other medications you could possibly require in addition to the study medications include antibiotics or other medications to manage side effects of treatment.

Ask the study doctor to discuss the costs that will or will not be covered by the sponsor. We encourage you to determine your health insurer's policy about paying for treatment in a research study. You and/or your medical/hospital insurance carrier will remain responsible for your regular medical care expenses.

WILL I BE PAID FOR PARTICIPATING?

You will not be paid for being in this research study.

WHO IS FUNDING THIS STUDY?

Pfizer is providing some of the funding for this research study. This means that the University of Iowa is receiving payments from Pfizer 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 Pfizer for conducting this study. The study drug is being provided by Sabinsa Corporation.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

- If you are injured or become ill from taking part in this study, medical treatment is available at the University of Iowa Hospitals and Clinics.
- The University of Iowa does not plan to provide free medical care or payment for treatment of any illness or injury resulting from this study unless it is the direct result of proven negligence by a University employee.
- If you experience a research-related illness or injury, you and/or your medical or hospital insurance carrier will be responsible for the cost of treatment.

WHAT ABOUT CONFIDENTIALITY?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that 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.

- federal government regulatory agencies,
- The U.S. Food and Drug Administration,
- Sabinsa Corporation and Pfizer, the study sponsors
- auditing departments of the University of Iowa, and
- the University of Iowa Institutional Review Board (a committee that reviews and approves research studies)

To help protect your confidentiality, we will use subject initials or unique identification code numbers only on data forms, have locked storage areas, and use password-protect computer files. If we write a report or article about this study or share the study data set with others, we will do so in such a way that

you cannot be directly identified.

The University of Iowa Hospitals and Clinics generally requires that we document your participation in research occurring in a University of Iowa Health Care facility. This documentation will be in either your medical record or a database maintained on behalf of the institution reflecting that you are participating in this study. The information included in the medical record will provide contact information for the research team as well as information about the risks associated with this study. We will keep this Informed Consent Document in our research files; it will not be placed in your medical record chart.

"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."

WILL MY HEALTH INFORMATION BE USED DURING THIS STUDY?

The Federal Health Insurance Portability and Accountability Act (HIPAA) requires your health care provider to obtain your permission for the research team to access or create "protected health information" about you for purposes of this research study. Protected health information is information that personally identifies you and relates to your past, present, or future physical or mental health condition or care. We will access or create health information about you, as described in this document, for purposes of this research study and for your treatment. Once your health care provider has disclosed your protected health information to us, it may no longer be protected by the Federal HIPAA privacy regulations, but we will continue to protect your confidentiality as described under "Confidentiality."

We may share your health information related to this study with other parties including federal government regulatory agencies, Pfizer, the University of Iowa Institutional Review Boards and support staff.

You cannot participate in this study unless you permit us to use your protected health information. If you choose *not* to allow us to use your protected health information, we will discuss any non-research alternatives available to you. Your decision will not affect your right to medical care that is not research-related. Your signature on this Consent Document authorizes your health care provider to give us permission to use or create health information about you.

Although you may not be allowed to see study information until after this study is over, you may be given access to your health care records by contacting your health care provider. Your permission for us to access or create protected health information about you for purposes of this study has no expiration date. You may withdraw your permission for us to use your health information for this research study by sending a written notice to Yousef Zakharia, M.D., University of Iowa Hospitals & Clinics, Department of Internal Medicine, 200 Hawkins Drive, C32 GH, Iowa City, IA 52242. However, we may still use your health information that was collected before withdrawing your permission. Also, if we have sent your health information to a third party, such as the study sponsor, or we have removed your identifying information, it may not be possible to prevent its future use. You will receive a copy of this signed document.

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. 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 Drop Out of the Study?

You are free to stop participating in this study at any time. If you stop, you will not lose any medical benefits except for any benefits that you might have been receiving in connection with this study. All information and samples collected from you before you stop the study may still be used by the study doctor or Sponsor.

If you want to stop participating in the study, please tell the study doctor. He can tell you about stopping all or part of the study activities and what other care is available 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 researchers or the study sponsor might decide to end your participation in this research study earlier than planned. This might happen because in our judgment it would not be safe for you to continue, because your condition has become worse, you need treatment not allowed by the study, because we have decided to stop the research, because you did not follow the study therapy regimen or because you may benefit from a new therapy.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: Dr. Yousef Zakharia at 319-356-4200. If you experience a research-related injury, please contact: Dr. Yousef Zakharia at 319-356-4200. If it is after 5 PM or on a weekend, call 319-356-1616 and ask for the Hematology/Oncology Fellow on call.

If you have questions, concerns, or complaints about your rights as a research subject or about research related injury, please contact the Human Subjects Office, 105 Hardin Library for the Health Sciences, 600 Newton Rd, The University of Iowa, Iowa City, IA 52242-1098, (319) 335-6564, or e-mail irb@uiowa.edu. General information about being a research subject can be found by clicking "Info for Public" on the Human Subjects Office web site, http://hso.research.uiowa.edu/. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Subjects Office at the number above.

This Informed Consent Document 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 signing this Informed Consent Document. 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 copy of this form.

CONSENT TO ARCHIVAL TUMOR SAMPLE:

I understand that I am being asked to provide an **archival** tumor tissue sample for research testing.

_____ (initial) Yes, I agree to participate in the Archival Tumor Tissue Sample

_____ (initial) No, I do NOT agree to participate in the Archival Tumor Tissue Sample

Subject's Name (printed): _____

Do not sign this form if today's date is on or after EXPIRATION DATE: 05/14/24.

_____ _____
(Signature of Subject) (Date)

Statement of Person Who Obtained Consent

I have discussed the above points with the subject or, where appropriate, with the subject's legally authorized representative. It is my opinion that the subject understands the risks, benefits, and procedures involved with participation in this research study.

_____ _____
(Signature of Person who Obtained Consent) (Date)