Subject ID # : 0004

NYU School of Medicine
NYU LANGONE MEDICAL CENTER

Perlmutter Cancer Center Clinical Trials Office

Informed Consent Documentation Checklist

☐ Initial
☐ Re-consent

Patient's Name: [redacted]
Last Name First Name

NYU Trial Number 14-01758 Sponsor protocol # (Industry trials) NP 29700

Date of Informed Consent 6/13/16

Protocol Version Date 03/JUN/2015

To be completed by the Research Nurse/Coordinator

Yes	No	N/A	Informed Consent Process	Comments
☒	☐		All questions raised by the patient and/or family members regarding the aforementioned trial and study participation were answered to their satisfaction	
☒	☐		The patient was counseled regarding the risks and benefits of the Investigational agent on this clinical trial to their satisfaction	
☒	☐		The current, IRB stamped version of the ICF was reviewed with the patient	
☒	☐		The patient signed the current ICF version dated 2/18/16 prior to undergoing any protocol specific procedures	
☒	☐		The patient initialed and date the ICF in all required fields	
☒	☐	☐	If applicable, any additional, optional or required consent information were completed (tissue studies, PK's, biomarkers, et cetera.)	
☒	☐		The investigator signed and dated the ICF	
☒	☐		The witness to the oral presentation printed, signed and dated the Informed Consent Document; **OR** Research Nurse/Coordinator entered "N/A" for the witness' printed name, signature and date when no oral presentation was required	
☒	☐		A signed copy of the ICF was given to the patient	
☒	☐		The Data Manager was notified that the patient signed the ICF	
☒	☐		Informed consent process was documented in patient's medical record by Investigator **(NOTE: Nurse Practitioners are not recognized as Investigators on NCI/Cooperative Group Trials)**	
			FOR NON-ENGLISH SPEAKING PATIENTS:	
☐	☐	☒	The ICF was verbally translated into the patient's native language and read out loud to patients, if not available in patient's native language Printed Name of Translator: _____ Translator ID Number: _____ Language of Translation: _____	
☐	☐	☒	The patient and interpreter signed and dated the translated "short form"	

Research Nurse's Signature [redacted] Date 6-13-16

Investigator Signature [redacted] Date 6/13/16

Version date: 1/30/2015

Subject ID # : 0004

NYU Langone MEDICAL CENTER

Research Subject Informed Consent Form

Title of Study:	**A PHASE IB, PROOF OF MECHANISM, OPEN-LABEL STUDY OF RO7070179, A HYPOXIA-INDUCIBLE FACTOR 1A (*HIF1A*) mRNA ANTAGONIST IN ADULT SUBJECTS WITH HEPATOCELLULAR CARCINOMA (HCC)** **NYU# S14-01758**
Principal Investigator:	**Jennifer Wu, MD** Dept. of Hematology and Medical Oncology Laura and Isaac Perlmutter Cancer Center New York University Langone Medical Center 462 First Ave, Bellevue Hospital, BCD 556 Telephone: 212-263-6485
Emergency Contact:	In an emergency, please contact Jennifer Wu, MD at 212-263-6485 and dial 911.

1. About volunteering for this research study

You are being invited to take part in a research study. Your participation is voluntary which means you can choose whether or not you want to take part in this study.

People who agree to take part in research studies are called "subjects" or "research subjects". These words are used throughout this consent form. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. You may also decide to discuss this study and this form with your family, friends, or doctor. If you have any questions about the study or about this form, please ask us. If you decide to take part in this study, you must sign this form. We will give you a copy of this form signed by you for you to keep.

2. What is the purpose of this study?

The purpose of this study is to see if an investigational drug RO7070179 is safe and can be useful in reducing the growth of Hepatocellular Carcinoma (HCC), a type of liver cancer. RO7070179 is considered investigational because it is not approved for sale (or general use) by the U.S. Food and Drug Administration (FDA) or other regulatory authorities for this purpose.

You are being asked to take part in this study because you have been diagnosed with HCC with normal to moderately impaired liver function.

Despite advances in surgery, liver transplantation, and newer drug therapies, the survival rate of subjects with HCC has improved only slightly over recent decades. Some laboratory studies and animal research suggest that RO7070179 shows anti-cancer activity by inhibiting (reducing or stopping) the growth of the tumor. It is designed to lower the amount of a protein called hypoxia-inducible factor-1 alpha (HIF-1α)

Subject ID # : 0004

that is elevated in many types of cancers that are resistant to chemotherapy and radiation therapy. However, it is not known if RO7070179 will lower the amount of HIF-1α in your cancer and if this will slow the growth of your cancer.

Approximately 100 patients with a variety of cancers have received this study medication to guide us to select a proper dose, but very few patients with liver cancer have been treated.

3. How long will I be in the study? How many other people will be in the study?

The study will be conducted at approximately 5 medical centers in the United States involving about 20 patients. Additional sites may be added to the study if required. We expect to enroll up to 12 patients in this study at NYU.

If you are enrolled into the study, you will be required to return to the clinic for approximately 15 visits (including the screening visit). You may need to attend additional visits, depending on how long you remain under treatment. The total duration for your involvement in the study (including the enrolment of all the subjects) may last up to 24 months.

If you don't respond adequately to treatment with RO7070179, treatment with RO7070179 will be discontinued. You will be required to return to the clinic for follow-up for 30 days after you discontinue from the study. This is to make sure there are no other side effects related to the drug and your health condition is stable. After that, information on your survival status will be collected every 3 months until study completion.

4. What will I be asked to do in the study?

Before any research procedures are done, you will be asked to read and sign this consent form. If you agree to participate in this study, you will undergo tests and procedures during a 4-Week Screening Period to determine if you are eligible to participate. If you are enrolled into the study, you will be required to return to the clinic for approximately 15 visits (including the screening visit). You may need to attend additional visits, depending on how long you remain under treatment.

This is an open label study where patients will receive doses of 13 mg/kg of RO7070179 as the study drug. "Open-label" means that you and the study doctor and study staff will know that you are receiving study drug. The dose of RO7070179 may be reduced if patients are not able to tolerate 13 mg/kg. The lowest dose to be tested is 6 mg/kg. If patients cannot tolerate 6 mg/kg, the study will be stopped.

You will be administered RO7070179 as a 2-hour intravenous (IV) infusion (given through a vein), on Days 1, 4, 8, 15, 22, 29 and 36 in the first cycle. Each cycle is 6 weeks. If you continue beyond 6 weeks of treatment, only one dose of RO7070179 will be given on the first day of each week in the second cycle and beyond. It is estimated each subject will receive 12 weeks of treatment if they do not have unacceptable side effects.

Based on the results obtained from the first 2 cycles, the principal investigator and representatives from the Sponsor will decide whether you should receive an additional cycle of RO7070179. After each additional cycle, the principal investigator and representatives from the Sponsor have to decide again whether treatment should be continued. The total duration for your involvement in the study (including the enrolment of all the subjects) may last up to 24 months.

Subject ID # : 0004

You can continue on treatment if clinical benefit is observed as judged by your study doctor and such treatment would continue as long as you experience this benefit until worsening of the disease, unacceptable side effects, or withdrawal of consent occurs.

WHAT TESTS AND PROCEDURES WILL BE USED IN THE STUDY?

You may be enrolled into the study after results of your screening procedures have been reviewed and approved by the study doctor and you meet the eligibility requirements. During these visits, you will undergo the procedures outlined below.

During the weekly dosing period of Cycle 1, you will be required to attend 7 clinic visits (Days 1, 4, 8, 15, 22, 29 and 36) and 6 clinic visits in subsequent cycles (Days 1, 8, 15, 22, 29 and 36). Refer to Table 1 on page 7 for the schedule of procedures to be completed during each visit. You may undergo some or all of the following procedures:

- Your medical history, demographics (age, gender, race) and height will be recorded (only at Screening).
- Physical examination (on Day 1 of each treatment cycle).
- Weight measurement (before the first RO7070179 dose of each treatment cycle).
- An evaluation of your ability to carry out daily activities (ECOG)
- Assessment of your vital signs including blood pressure, breathing rate, pulse, and oral temperature (at all visits).
- An electrocardiogram (ECG - a painless recording of the electrical activity of your heart) will be performed (only during the screening period).
- Urine samples will be collected for pregnancy testing (all female subjects – at screening), urine screen for drugs, alcohol, and to assess your kidneys, and for tests that will possibly enable us to better understand the course of your disease.
- Blood samples for clinical laboratory tests will be collected to assess your kidneys, liver, and how many blood cells are in your blood.
- Blood samples will also be collected for biomarker tests that will possibly enable us to better understand the course of your disease (Biomarkers (proteins) are indicators of disease processes and treatment response.) For instance alpha fetoprotein [AFP], a protein that is made by hepatocellular cancer, is a HCC biomarker that will be measured along with other biomarkers.
- You will be asked for details about any medication you have taken since your last visit (every week).
- You will be asked about your general health since your last visit (every week).
- During your first cycle (Cycle 1) you will receive an intravenous infusion of RO7070719 on Days

1, 4, 8, 15, 22, 29 and 36. For any additional cycles (Cycle 2 and beyond) you will receive an intravenous dose of RO7070719 on Days 1, 8, 15, 22, 29 and 36.

- Blood sampling will be performed to determine the amount of RO7070179 in your blood, called pharmacokinetic (PK) analysis.
  - On Day 1 of Cycle 1, you will have blood taken predose (within 15 to 30 minutes before the start of the infusion);
  - at 30 and 60 minutes after the start of infusion;
  - within 15 minutes before the end of the infusion;
  - 10 minutes, 30 minutes, and 1, 2, 4, 6, 72 and 168 hours after the end of the infusion.
  - Another set of blood samples will be taken at Day 36 (Week 6) predose (within 15 to 30 minutes before the start of the infusion);
  - at 30 and 60 minutes after the start of infusion;
  - within 15 minutes before the end of the infusion;
  - 10 minutes, 30 minutes, and 1, 2, 4, and 6, hours after the end of the infusion.

To make the blood collection easy for you, a special blood collection catheter (tube) may be placed in your vein, and this may stay in your vein until all blood samples are taken. If a catheter is placed, the blood samples will be taken from the catheter. The catheter will be removed from the vein after the last blood sample is taken.

- Blood sampling will be performed to determine whether RO7070179 has effects against the cancer in your body, called pharmacodynamics (PD) analysis. Samples will be collected at Weeks 1 and 4 for Cycle 1 and at Week 1 for subsequent treatment cycles. Effects will be measured on AFP, and additional biomarkers.

- Part of the blood samples collected for PK and PD measurements may be used for additional purposes: immunogenicity testing (test the ability of the molecule to provoke an immune response), assessment of protein binding, interactions with other plasma components or assay development.

- Blood will also be collected to see if RO7070179 affects the ability of your blood to form clots. This will be done on the first infusion of treatment Cycle 1, before the study drug is given, and at 1 hour after the end of infusion. For all of the other visits, this will be done before the infusion of the study drug.

- You will be asked to undergo two biopsies (sampling of tumor tissue) to obtain tumor tissue from your liver. Both biopsies are mandatory. One biopsy will be between the time you provide informed consent for the study and the first dose of study drug, and the second biopsy will be at Week 6 of Cycle 1. A biopsy procedure will involve removing a part of your tumor. The biopsy can be taken with a needle or by a small surgery, and it is usually done with local or general anesthesia (shots to numb the skin). You may or may not also receive sedation (drugs to make you sleepy).

Subject ID #: 0004

- Before each biopsy, an imaging technique called Dynamic Contrast Enhanced Magnetic Resonance Imaging (DCE-MRI) will be used to identify regions of low blood flow (hypoxia) in the tumors. A contrast (dye) will be injected into a vein prior to the scan in order to enhance the images. Signing this consent means you agree to participate in this study as well as undergo these biopsies. Tissue from the biopsies will be studied to determine if RO7070179 has certain effects on the tumor.

- Additional tumor assessments will be done using Magnetic resonance imaging (MRI) and Computed Tomography (CT). MRI uses magnetic fields to create images of the structures inside your body while CT uses x-rays to make these images. These assessments will be done at Screening, Week 12 (after Cycle 2) and every 2 cycles after that.

- If you decide to choose not to continue your participation, or if the doctor asks to you stop taking the medication, regardless of the reason of your discontinuation, you will be required to return to the clinic for follow-up for 30 days after you discontinue from the study. This is to make sure there are no side effects related to the drug and your health condition is stable. These updates may be either in person at a clinic visit or through communication with you or your doctor.

STUDY COMPLETION OR EARLY TERMINATION

If you complete the study, choose to withdraw from this research study, or your participation is terminated (ended) by your doctor or the Sponsor for any reason, you will be asked to come to the clinic for a completion visit approximately 30 days after receiving your last dose of RO7070719 or after the decision was made to discontinue RO7070719.

At this visit, the following assessments will be performed:

- A complete physical examination, including recording the weight.
- An evaluation of your ability to carry out daily activities (ECOG)
- Assessment of your vital signs including blood pressure, breathing rate, pulse, and oral temperature
- A tumor assessment (using CT) will be performed.
- You will be asked to report any symptoms and health problems you have and any new medications or changes in existing medications that you are taking.
- Blood will be collected to measure the ability of your blood to form clots and for safety laboratory tests (blood counts, liver and kidney function)
- Blood will be collected to test for AFP.
- Your vital signs will be measured and your weight will be measured again.
- An ECG will be performed to measure the electrical activity of your heart.
- A sample of your urine will be collected for standard laboratory tests.

With the blood tests, an estimated amount of blood that will be taken from you, if you agree to receive two treatment cycles are shown below. Note that 5 milliliters (5mL) is about 1 teaspoon (tsp) and 3 teaspoons = 1 tablespoon. 500 mL is the amount of blood taken when someone donates one unit (one

Subject ID#: 0004

pint)(two cups) of blood in a blood bank.

Estimated Total Amount of Blood Taken During the Study:

Time Point in the Study	Type of Blood Testing	Estimated Total Amount of Blood Taken
Screening	Routine Lab test	30 mL (6.0 tsp or 2 tbsp)
Treatment Cycle 1	Routine Lab test, PK and PD	150 mL (30.0 tsp or 10 tbsp)
Treatment Cycle 2	Routine Lab test, PK and PD	90 mL (18.0 tsp or 6 tbsp)
End of Treatment	Routine Lab test, PK and PD	40 mL (8.0 tsp, about ½ tbsp)
Estimated Total Amount of Blood Taken During About 12 Weeks		**310 mL (62 tsp) (less than 1 ½ cup)**

A total of about 14 needle insertions with a total amount of around 310 mL will be collected over 2 treatment cycles during the study course.

Schedule of Events:

	Screening[1]	Treatment Cycle 1[2]							Treatment Cycle ≥ 2						End of Treatment[3]
		Baseline (Day 1)	Day 4	Day 8	Day 15	Day 22	Day 29	Day 36	Day 1	Day 8	Day 15	Day 22	Day 29	Day 36	
				Wk 2	Wk 3	Wk 4	Wk 5	Wk 6	Wk 1	Wk 2	Wk 3	Wk 4	Wk 5	Wk 6	
RO7070179 administration		X	X	X	X	X	X	X	X	X	X	X	X	X	
Informed Consent	X														
Medical history	X														
Physical examination	X	X							X						X
Demographics and height	X														
Weight	X	x							x						X
ECOG performance status	X	X							X						X
Pregnancy test	X														X
Vital signs[7]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Hematology with differential, platelets	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Serum chemistries	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Coagulation panel	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
HBV-DNA, HCV-RNA	X														
Urinalysis	X	X							X						X
12-Lead ECG	X														X
Assessment of AEs/toxicity	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant medications and procedures	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pharmacokinetics		X	X	X				X							
Pharmacodynamics – AFP		X				X			X						X
Pharmacodynamics – paired tumor biopsies	-14 to -1							X							
DCE-MRI	X							X							
Contrast CT assessment of tumor response every 2 cycles	X													X	X

Subject ID #: 0004

Subject ID#: 0004

WHAT ARE MY RESPONSIBILITIES?

During the study you will have the following responsibilities:

- Attend all scheduled visits on time.
- Notify the study doctor or study staff of any illnesses or injuries, unexpected or troublesome side effects, or problems that occur.
- Notify the study doctor if you plan to have an elective surgery (surgery that is scheduled in advance) or any other medical treatment or procedure.
- Notify the study doctor or study staff of changes in medications and do not take any medication without the approval of the study doctor.
- Not participate in another clinical research study during this study.

WHAT ARE YOUR RESTRICTIONS DURING THE STUDY?

You will be required to adhere to the following restrictions while taking part in this study:

- You must continue to use adequate birth control methods as previously stated.
- You must not use any other therapies known or suspected to potentially impact the investigational drug during this study.
- Participation in any other investigational drug study is prohibited during this study.

Subject ID #: 0004

5. What are the possible risks or discomforts?

Risk of Study Drug

We do not know all of the side effects of the study drug RO7070179.

The most common events noted in the previous studies using RO7070719 are:

- Tiredness (fatigue)
- Decrease in red blood cells (anemia), which can cause fatigue and shortness of breath.
- Vomiting sensation (nausea)
- Abnormal liver enzymes (tests that measure liver function)
- Chills
- Rash
- Feeling full after eating
- Diarrhea
- Headache
- Loss of appetite (anorexia)
- Pain in the joints or muscles
- Fever
- Dry skin
- Itching
- Swelling of the moist lining inside the mouth or other linings in the body

So far, the following other events of RO7070179 have been reported rarely:

- Back pain
- Constipation
- Decreased sodium in your blood
- Difficulty in sleeping
- Hiccups
- Increased sensitivity to stimulation, especially touch
- Involuntary leakage of urine
- Loss of taste
- Night sweats
- Pain in hands and/or feet
- Ringing in the ears
- Swelling of muscles
- Weakness of muscles
- Balance disorder
- Decrease in proteins that affect your ability to form clots or stop bleeding
- Difficulty in breathing
- Gas
- Increased blood pressure
- Infusion-related reaction
- Lack of ability to urinate
- Muscle spasms
- Pain at the infusion site
- Redness of the skin
- Swelling of hands and/or feet
- Tingling and numbness in hands and/ or feet

Subject ID # : 0004

It is very important that you tell the study doctor and the study staff about any side effects that you may have experienced.

You may experience side effects or discomforts that are not listed on this form. Tell your study doctor or study staff immediately if you have any problems. Your safety will be closely monitored during the course of the study.

Other Risks

Side Effect of Having Blood Taken

Fainting or feeling faint. Tell the study staff right away if you feel faint. Redness, pain, bruising, bleeding or infection at the needle site.

Vital Signs

When your blood pressure is taken, it is possible for the blood pressure cuff to cause discomfort or bruising to the upper arm.

Electrocardiogram (ECG)

The ECG test is a recording of the electrical activity of your heart and an ECG harmless. The sticky pads (electrodes) that are placed on your chest can sometimes cause discomfort such as redness or itching. We may need to shave your chest before we attach these pads. Irritation from shaving also may occur.

Magnetic Resonance Imaging (MRI)

Magnetic Field Risk:

MRI uses a strong magnetic field to create images of the body. Because of the strong magnetic field, there are risks. These risks are detailed in this section.

One possible risk is burns to the skin. There is an increased risk of burns from devices that conduct electrical energy. These devices can include metallic objects, pulse oximeters, EKG leads, or skin tattoos. These devices can be either in or on the patient in order for a skin burn to occur. The FDA has found that 70% of all reported injuries from MRIs were burns to the skin.

To reduce this risk, all patients who are scanned in this study must complete thorough screening to ensure that no conductive materials are present in or on the patient's body. Additionally, the power limits of the magnet will adjusted as necessary.

Another possible risk is that a metal object could be pulled into the scanner and hit you. You could be physically injured as a result.

To reduce this risk, everyone near the magnet will remove all metal from their clothing or pockets when in the scanning environment. The door to the scan room will remain closed during the exam for your safety.

There are no known risks or adverse effects resulting directly from exposure to MRI. However, subjects who have a pacemaker or metal objects in their body such as shrapnel or metal in the eye should not

Subject ID#: 0004

have the scan performed. If you have any question about metal implants or metal fragments in the body, you should inform the technologist or investigators before entering the magnet room.

Fear of Confined Spaces: Some people may feel confined and experience anxiety in the MR scanner. If you are unable to tolerate being in the scanner, we can stop the scan immediately at any time.

Noise Levels: The MR scanner produces tapping sounds during operation, which may reach very loud levels. To minimize any discomfort from this noise, you will be given disposable earplugs to reduce the noise levels but will still allow voice communication with the scanner operator.

MRI system failure (quench): In extremely rare cases, a magnet can lose its magnetism, in which case cooling fluids may be released noisily through escape valves and may collect in gas form in the scan room. The gas is not harmful in itself as long as fresh air is available. In this very remote event, you will immediately be brought out of the magnet room.

Neurostimulation and heating: Some subjects may experience muscle twitches or tingling sensations and/or a slight increase in body temperature during some types of scan activity. These are very unlikely under current MR guidelines.

For Studies Requiring Gadolinium Contrast Material: The FDA approves the imaging agent gadolinium for use in MRI. Some subjects, (less than 3%) may experience minor discomforts that include nausea and /or headache after injection. These side effects usually pass quickly without medical treatment.

Risk of NSF: In a small number of cases, a condition known as NSF or nephrogenic systemic fibrosis has been linked to gadolinium in subjects with a history of moderate to severe kidney disease. Subjects with a history of moderate to severe kidney disease will be required to undergo a blood test prior to receiving gadolinium to verify adequate kidney function.

Pregnant patients: Gadolinium-DTPA should not be administered to pregnant patients. If there is a possibility that you could be pregnant, you will be asked to undergo a pregnancy test before being allowed to participate in this study.

Risks to the intravenous injection of gadolinium include bleeding or bruising around the injection site, and rarely, infection.

Liver Tumor Biopsy

You may feel some amount of pain or discomfort during the biopsy, including slight, stinging pain when a local anesthetic is injected by needle to numb the area where the biopsy needle is inserted, pressure and dull pain and allergic reaction to the medication used to numb the location where the biopsy needle is inserted and soreness at the biopsy site.

If pain after the biopsy makes you uncomfortable, you may be given a pain medication by your study doctor. A biopsy of the tumor in your liver is not considered to be a major procedure although there is a small chance of serious post-procedure complications, such as infection, fever, swelling or internal bleeding (hemorrhage). The death rate from such complications is 1 in 10,000 patients undergoing a tumor biopsy. Your study doctor will explain the details of the procedure and the risks to you.

The following procedures are considered part of your regular care and would be done even if you were not in the study: physical exams, routine blood tests, and CT scans.

Your doctor(s) will explain the risks associated with these procedures. If sedation is needed for the tumor liver biopsy, your doctor will explain the risks involved with this procedure to you.

6. Can I be in the study if I am pregnant or breastfeeding?

Reproductive Risks

The effects of RO7070179 on human pregnancy and the unborn child (fetus) are unknown. **Therefore, it is very important that you do everything within your power not to become pregnant, or father a child during this study and for 6 months after the end of study treatment.** Please ensure that you follow the study birth control requirements outlined in the sections regarding information for male and female volunteers above.

If you become pregnant during the course of the study, you will be withdrawn from the study. Neither the clinic nor the Sponsor will be responsible for the cost of any obstetric or related care, or for your child's care. By signing this consent, you are agreeing that the outcome of any pregnancy that occurs during this study will be reported to the Sponsor. The Sponsor may request access to both you and your child's medical records for a minimum of 8 weeks following delivery.

If neither you nor your partner is surgically sterile or if you have not reached menopause (absence of menstrual periods for at least 2 years), you are required to use highly effective methods of birth control suggested by your study doctor such as:

- Hormonal methods like birth control pills, patches, vaginal rings or implants,
- Double barrier methods such as condom plus diaphragm or a diaphragm used with spermicide (a foam, cream or gel that kills sperm),
- Intrauterine device (IUD),
- Abstinence (no sex).

If you think you may have become pregnant even though you used correct contraception while in the study, you should immediately contact the study doctor and must tell your obstetrician or other health care provider caring for you during your pregnancy that you took part in this study. A positive blood test for pregnancy will require immediate stopping of study medication, and you will be discontinued from the study for safety reasons.

- Men should not plan to have babies with their wives, partners, or significant others while taking part in this study. Female partners of male patients must also adhere to similar birth control methods as described for women patients in this study.

- All patients should continue to use the above methods of birth control to prevent pregnancy for 6 months after the last dose of RO7070179

Note to Men

Because the effect of participating in this study on sperm are unknown, you will be required to use a medically accepted method of birth control while you participate in the study and for 6 months after the end of study treatment, using one of the methods described above.

If your partner becomes or thinks she may have become pregnant during the time you are in the study or within 6 months after, you must tell the principal investigator right away. The principal investigator may ask for your partner's permission to collect information about the outcome of her pregnancy and the health of her baby. You will be given a contact form to share with your partner so that she can reach out to the study team if she is interested in providing information about her pregnancy and the health of her baby.

By sharing the contact form with your partner, your partner will become aware of your participation in this study. If your partner chooses to provide her and her baby's health information, she will be asked to sign a consent form before this information is collected.

7. What if new information becomes available?

During the course of this study we may find more information that could be important to you. This includes information that might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

8. What are the possible benefits of the study?

You may receive no benefit from receiving RO7070179 in this study

By taking part in this research study, you may be helping future patients by providing important information about RO7070719 and by contributing to medical knowledge.

9. What other choices do I have if I do not participate?

You do not have to participate in this study. You can get treatment or care for your illness even if you are not in a research study. Your study doctor can tell you more about these treatments. However, since you have progressed or not tolerated other standard treatments, your choice is limited to investigational medications or you may also choose not to receive any treatment for the cancer and just receive supportive treatment.

The length of treatment for the alternative regimen depends on how well you respond.

While you are on this study, you will not receive other investigational treatments.

If you decline to take part in this study, your decision will not prevent you from receiving additional treatments according to the standard of care as determined by your doctor.

10. Will I be paid for being in this study?

Your participation in this study is voluntary and you will not receive any compensation for your participation.

11. Will I have to pay for anything?

You and/or your health insurance may be billed for the costs of medical care during this study if these expenses would have happened even if you were not in the study. If you have health insurance, the cost of these services will be billed to your insurance company. If your insurance does not cover these costs

or you do not have insurance, these costs will be your responsibility. You and your health insurance will be responsible for:

- physical exams
- routine blood tests
- CT scans

The study drug, RO7070179, and study-related tests, such as: blood test for hepatitis ECG, MRI, the collection of tumor samples for analyses, blood samples for pharmacokinetic, biomarker and antibody and genetic testing will be paid by the sponsor.

12. What happens if I am injured from being in the study?

For medical emergencies contact 911. If you think you have been injured as a result of taking part in this research study, tell the principal investigator as soon as possible. The principal investigator's name and phone number are listed at the top of page 1 of this consent form.

It is important that you follow carefully all the instructions given by the study doctor and his/her study staff regarding this study.

If you become ill or are physically injured as a result of participation in this study, the study doctor will treat you or refer you for treatment.

Reasonable costs of such treatment beyond that provided by a third party such as your insurance will be covered by the Sponsor, Roche if:

- you received reasonable medical care;
- you followed instructions;
- the injury is directly related to the properly administered investigational study drug;
- the injury is not the result of the natural course of any underlying disease and/or pre-existing disease process present prior to the proper administration of investigational study drug

You will not be compensated for other injury or illness-related costs such as lost wages.

Federal law requires Roche to inform the Centers for Medicare & Medicaid Services (CMS, the agency responsible for administration of the Medicare program) when Roche is going to reimburse for patient injury expenses for treatment of an injury to a Medicare beneficiary. To comply with a Medicare reporting obligation, Roche or its representative may need to collect and share with CMS certain personal information about you, such as your name, date of birth, sex, social security number, and Medicare ID number (if you have one).

There are no plans for the NYU School of Medicine or Medical Center to pay you or give you other compensation for the injury. In no way does signing this consent form waive your legal rights nor does it relieve the study doctors, Sponsor, or involved institutions from their legal and professional responsibilities.

13. When is the study over? Can I leave the Study before it ends?

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped or your participation ended at any time by your physician, the study sponsor, or the Food and Drug Administration (FDA) without your consent because:

- The principal investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- You become pregnant
- You need treatment not allowed in this study;
- The study sponsor, the principal investigator, the Food and Drug Administration (FDA) or other body responsible for monitoring the safety of the study has decided to stop the study.

If you decide to participate, you are free to leave the study at anytime. Leaving the study will not interfere with your future care, payment for your health care or your eligibility for health care benefits.

If you decide to leave the study or are withdrawn from the study, your participation in the study will end and the study staff will stop collecting information from you; however, you will be asked to come back to the clinic for an end of study visit for safety reasons. Your samples will be destroyed at the end of the study. However, Roche will continue to retain and use any research results that have already been collected to verify the scientific integrity of the study. If you wish to leave the study, inform your study doctor.

14. How will my information be protected?

NYU Langone Medical Center, which includes NYU Hospitals Center and NYU School of Medicine, is committed to protecting the privacy and confidentiality of your health information. We are asking for your permission to use and to disclose your health information in connection with this study. You have the right not to give us this permission, in which case you will not be able to participate in this study. If you do not give this permission, your treatment outside of this study, payment for your health care, and your health care benefits will not be affected.

What information about me may be used or shared with others?
The following information may be used or shared in connection with this research:

- Information in your medical record and research record, for example, results from your physical examinations, laboratory tests, procedures, questionnaires and diaries.

You have a right to access information in your medical record. In some cases when necessary to protect the integrity of the research, you will not be allowed to see or copy certain information relating to the study while the study is in progress, but you will have the right to see and copy the information once the study is over in accordance with NYU Langone Medical Center policies and applicable law.

Why is my information being used?
Your health information will be used by the research team and others involved in the study to conduct and oversee the study.

Subject ID #: 0004

Who may use and share information about me?
The following individuals may use, share or receive your information for this research study:

- The Principal Investigator, study coordinators, other members of the research team, and personnel responsible for the support or oversight of the study.
- The study sponsor: Roche Pharmaceuticals and third parties working with the Sponsor
- Governmental agencies responsible for research oversight (e.g., the Food and Drug Administration or FDA).
- Health care providers who provide services to you in connection with this study, and laboratories or other individuals who analyze your health information in connection with this study.
- Other study sites

Your information may be re-disclosed or used for other purposes if the person who receives your information is not required by law to protect the privacy of the information.

How long may my information be used or shared?
Your permission to use or share your personal health information for this study will never expire unless you withdraw it.

Can I change my mind and withdraw permission to use or share my information?
Yes, you may withdraw or take back your permission to use and share your health information at any time. If you withdraw your permission, we will not be able to take back information that has already been used or shared with others. To withdraw your permission, send a written notice to the principal investigator for the study noted at the top of page 1 of this form. If you withdraw your permission, you will not be able to stay in this study.

15. Optional permission for future use

NYULMC would also like to store, use, and share your health information from this study in research databases or registries for future research conducted by NYULMC or its research partners. Such health information may include biological samples from the study. To give this additional permission, check the box below and write your initials where indicated. You may still participate in this study even if you do not give us this additional permission.

NYULMC will continue to protect the confidentiality and privacy of this information as required by law and our institutional polices. If you give this additional permission, you will continue to have the rights described in this form. You have the right to take back this additional permission at any time.

☐ Checking this box indicates my permission to store, use, and share my health information from this study in research databases or registries for future research conducted by NYULMC or its research partners. _____ Subject Initials

16. The Institutional Review Board (IRB) and how it protects you

The IRB reviews all human research studies – including this study. The IRB follows Federal Government rules and guidelines designed to protect the rights and welfare of the people taking part in the research studies. The IRB also reviews research to make sure the risks for all studies are as small as possible. The NYU IRB Office number is (212) 263-4110. The NYU School of Medicine's IRB is made up of:

Subject ID# : 0004

- Doctors, nurses, non-scientists, and people from the Community

17. Who can I call with questions, or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on top of the page 1 of this consent form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Institutional Review Board (IRB) at (212) 263-4110.

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

When you sign this form, you are agreeing to take part in this research study as described to you. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer.

[redacted]

Name of Subject (Print)

[redacted]

Name of Person Obtaining Consent (Print)

[redacted] Obtaining Consent

6/17/16

Subject ID #: 0004

Witness to Consent of Non-English Speaking Subjects Using the "Short Form" in Subject's Spoken Language

Statement of Witness
As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

[redacted]

Name of Witness (Print) | Signature of Witness | Date

Witness to Consent of a Subject Who Cannot Read or Write

Statement of Witness
I represent that the consent form was presented orally to the subject in the subject's own language, that the subject was given the opportunity to ask questions, and that the subject has indicated his/her consent and authorization for participation by (check box that applies).

- ☐ Subject making his/her own "X" above in the subject signature line
- ☐ Subject showed approval for participation in another way; describe:

[redacted]

Name of Witness (Print) | Signature of Witness | Date