RESEARCH PATIENT INFORMATION AND CONSENT FORM	
TITLE:	**A Parallel Phase 2 Study of Glesatinib, Sitravatinib or Mocetinostat in Combination With Nivolumab in Advanced or Metastatic Non-Small Cell Lung Cancer**

This consent form contains important information to help you decide whether to participate in this research study.

The study staff will explain this study to you. Ask questions about anything that is not clear at any time. You may take home an unsigned copy of this consent form to think about it and discuss it with family or friends.

- **Being in this study is voluntary – <u>your choice</u>.**
- **If you join this study, you can still <u>stop at any time</u>.**
- **<u>No</u> one can <u>promise</u> that a study will help you.**
- **Do not join this study unless all of your <u>questions</u> are <u>answered</u>.**

After reading and discussing the information in this consent form you should know:

- Why this research study is being done;
- What will happen during the study;
- Any possible benefits to you;
- The possible risks to you;
- Other options you could choose instead of being in this study;
- How your personal health information will be treated during the study and after the study is over;
- Whether being in this study could involve any cost to you; and
- What to do if you have problems or questions about this study.

<u>Please read this consent form carefully.</u>

TITLE: **A Parallel Phase 2 Study of Glesatinib, Sitravatinib or Mocetinostat in Combination With Nivolumab in Advanced or Metastatic Non-Small Cell Lung Cancer**

PROTOCOL NO.: MRTX-500

SPONSOR: Mirati Therapeutics, Inc.

INVESTIGATOR: *Enter PI name*

SITE(S): *Enter addresses of all locations to be used*

STUDY-RELATED PHONE NUMBER(S): *Contact Name*
Telephone Number (24 hours)

Patient's Name: _____ Medical Record Number: _____

INVITATION TO PARTICIPATE IN A RESEARCH STUDY

You are being asked to take part in a clinical research study at [enter site name]. This consent form explains why this research study is being performed and what your role will be if you choose to participate. This form also describes the possible risks related with taking part in this study.

You are being asked to take part in this study because you have a diagnosis of advanced or metastatic lung cancer, for which the proposed study treatment is a reasonable next treatment or because there are no standard therapies beyond those you have already received.

Before agreeing to participate in this research study, it is important that you read and understand the following explanations of the study and the proposed study procedures. Clinical studies include only patients who choose to take part. Please take your time to make your decision. Ask the study doctor or the study staff to explain any words in this document that you don't understand. Make sure that all your questions have been answered to your satisfaction. If you decide to participate in this study, you will be asked to sign this consent form to confirm that you have been informed of the nature of the study and what it involves.

A description of this clinical study 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.

PURPOSE OF THE RESEARCH STUDY

WHY IS THIS STUDY BEING DONE?

This is a study of 3 different investigational (experimental) drugs given in combination with the immunotherapy nivolumab (also known as OPDIVO®). Immunotherapy is treatment that uses your body's own immune system to help fight cancer. The 3 investigational drugs are being developed by Mirati Therapeutics, Inc., which is the company that will provide these drugs. "Investigational" means that the drugs are being tested but have not been proven to help patients with the disease you have and are not approved by the U.S. Food and Drug Administration (FDA). Nivolumab is an FDA approved agent and is made by Bristol Myers Squib. The study is being funded and organized by Mirati Therapeutics, Inc.

This study will evaluate if patients with non-small cell lung cancer will benefit from treatment by adding any of the investigational drugs to nivolumab. The study will enroll patients into 3 groups, each testing a different investigational drug in combination with nivolumab. Your study site has been assigned to enroll patients into the group that will receive nivolumab in combination with the investigational agent sitravatinib. This consent form will describe what to expect with sitravatinib and nivolumab.

Other objectives of the study include assessing how quickly the investigational drugs are absorbed into the blood stream and how fast they are removed. Several laboratory tests will be

performed using samples of tumor tissue or blood to understand how and why the drugs may work together in the treatment of lung cancer.

BACKGROUND – SITRAVATINIB AND NIVOLUMAB

Sitravatinib is an experimental drug that belongs to a class of drugs known as tyrosine kinase inhibitors. Sitravatinib is being developed as a possible treatment for different types of cancer.

Sitravatinib is designed to block specific proteins that are thought to cause tumors to grow and to prevent growth of new blood vessels that help cancer tumors to grow and spread. In addition, research indicates that sitravatinib may help stimulate a patient's immune system, improving its ability to recognize and attack cancer cells.

Nivolumab is an FDA approved, prescription drug that belongs to a class of drugs known as checkpoint inhibitors; specifically, nivolumab is an inhibitor of the Programmed Cell Death (or PD-1). Cancers can have extra signal molecules (PD-L1 molecules) on their surface that make the immune system accept them as normal, helping the cancer cells avoid attack by the immune system. Nivolumab can block these signal molecules, allowing the immune system to recognize and attack cancer cells.

This study will evaluate whether the combination of immune system stimulation caused by sitravatinib and improved recognition of tumor cells caused by nivolumab results in more anti-tumor activity (tumor shrinkage) than would be expected with either agent used alone.

DESCRIPTION OF THE RESEARCH STUDY

The study for sitravatinib plus nivolumab will include groups of patients with non-small cell lung cancer, including patients who have previously received prior treatment with a checkpoint inhibitor (as many as 125 patients) and patients who have not previously received treatment with a checkpoint inhibitor (as many as 61 patients). Including all investigational treatment groups and sub-studies, as many as 25 study sites in the United States and 280 patients are expected to participate in this study.

WHAT HAPPENS BEFORE ANY TREATMENT?

Screening Tests

Before you can enroll in the study, screening tests will be done to help the study doctor decide if you are eligible to take part in this study.

The following tests and procedures will be performed during screening:

- Your complete medical history will be recorded, including any cancer treatments you may have previously received.
- You will be asked how well you are able to perform the normal activities of daily living.

- You will be asked about any other medications you are taking, including over the counter medications and natural supplements.
- You will have a full physical exam, including measurement of your vital signs (blood pressure, pulse rate, and temperature), weight and height.
- Blood (about 3 teaspoons) and urine will be collected for routine tests and a test to ensure your blood is clotting normally. This may be repeated at other times during the study if your study doctor feels it is necessary.
- Blood (about 2 teaspoons) will be collected to measure markers of the immune system (biomarkers) that may change during treatment.
- Women who are able to have children will have a blood (about 1 teaspoon) or urine pregnancy test. This may be repeated at other times during the study if your study doctor feels it is necessary.
- You will have an electrocardiogram (ECG), which is a test that shows how the heart is working by measuring its electrical activity.
- You will have an echocardiogram (ECHO, an ultrasound of the heart) to evaluate the pumping function of your heart.
- You will have a computed tomography (CT) scan, a whole body bone scan and a magnetic resonance imaging (MRI) brain scan to evaluate any tumor(s) before treatment. Depending on the status and location of the tumor(s), other scan methods may be used instead. This will be determined by your study doctor.

Collection of Tumor Samples to Test for Immune System Markers

For patients who have not received prior checkpoint inhibitor treatment, testing of your tumor collected after your most recent treatment is necessary for study entry. This testing is not optional. Whether your tumor has no/low or high PD-L1 signal molecule expression must be known to enter the correct study group. If the same test has been performed recently for a different purpose, the results may be adequate to meet the needs of the study and permission to use the information is requested. You may have tumor tissue already available from a recent biopsy or procedure performed since your last treatment. If you have not had a recent biopsy, you will need to have a new biopsy to obtain a sample. Your study doctor will describe what to expect in your case.

For patients who have received prior checkpoint inhibitor treatment, the researchers conducting this study would like to send samples of your tumor to central laboratories to be tested for PD-L1 signal molecule expression and other immune system markers before you start study treatment and again during treatment. These experimental markers may help researchers understand whether and how sitravatinib and nivolumab work together to treat cancer, and which future patients with cancer may benefit the most from treatment with sitravatinib and nivolumab in combination. This testing is not required for study entry but is very valuable in learning how and why the combination therapy may be effective in treating cancer. If the same test has been performed recently for a different purpose, the result may be enough to meet some of the needs

of the study and permission to use the information is requested. You may have tumor tissue already available from a recent biopsy or procedure performed since your last treatment. If you have not had a recent biopsy or surgery, you may be asked to have a new biopsy to obtain a sample. You study doctor will describe what to expect in your case.

Collection of Blood for Tumor Gene Testing

In addition to the immune system tests described above, the researchers conducting this study would like to send samples of your blood to central laboratories to test for changes in the genetic molecules from the tumor. Genes are forms of DNA that are passed along as cells multiply; the genes tell the cells how to grow and function. The genes from tumors are not those that are passed from parent to child and determine things like hair and eye color. Gene molecules (DNA) from the tumor can be found not only in tumor tissue but also in the blood. These molecules were originally in tumor cells but have been released and are now circulating in the blood. Circulating tumor DNA (ctDNA) cannot start the growth of new tumors but can be used to test for gene changes. The tests for ctDNA and genes in the tumor tissue will help researchers know whether your tumor has gene changes (increased number of copies or mutations) that may be targeted by the investigation study treatment in addition to possibly helping nivolumab be effective.

Your blood samples for ctDNA testing and tumor tissue sample will be kept for a maximum of 10 years, after which they will be destroyed; however, you may request at any time that your samples be destroyed earlier, if you wish to do so. Your samples will only be identified by a unique study number. However, even if you were not eligible to participate in the study, limited information about your case may be collected to help interpret any findings (e.g. your age, gender, type of cancer, and information on your prior treatments). This will allow the researchers to study future questions about the cancer disease and study drug.

WHAT HAPPENS DURING TREATMENT?

Study Drug Regimen

Sitravatinib capsules will be taken by mouth once every day. Nivolumab infusions will be administered by intravenous infusion (infusion of the liquid medication directly into your vein) either once every 2 weeks or once every 4 weeks. Your study doctor will discuss which dosing is best for you. If you experience side effects, or your doctor or study team notices abnormal findings in your lab or EKG results, your dosing regimen of both sitravatinib and nivolumab may be interrupted. Treatment is divided into cycles; each cycle is 28 days in length.

Study Drug Administration

Sitravatinb will be provided as capsules. The dose of sitravatinib that you will receive will be based on the experience of people treated in the study before you. Your study doctor will tell you the dose of sitravatinib to expect. You will take sitravatinib once daily. You may receive different strengths of sitravatinib capsules to make the right dose. The study doctor or nurse will tell you exactly how many capsules of each strength to take. If you experience intolerable side

effects, your dose of sitravatinib may be lowered. Both you and your doctor will know which dose of sitravatinib you will receive.

- Sitravatinib capsules should be taken on an empty stomach at least 2 hours after the previous meal and 1 hour before the next meal.
- You will swallow the sitravatinib capsules with at least 200 mL (less than 1 cup) of water.
- Sitravatinib capsules should be swallowed whole and not be chewed.
- If you miss a dose or vomit after taking a dose, you should not make up the dose and do not double up the next dose.
- You will be given a diary card by the study staff for each sitravatinib treatment cycle. You should record each time you take sitravatinib capsules, and any missed doses on the diary card. Take the diary card with you to every clinic visit. At the end of each treatment cycle, the study staff will collect the diary card to keep in the study records.

Nivolumab will be administered by intravenous infusions (infusion of the liquid medication directly into your vein). Either the standard flat dose of 240 mg will be administered in the clinic every 2 weeks or the standard flat dose of 480 mg will be administered in the clinic every 4 weeks. The infusions will last about 30 minutes. Your study doctor will discuss which dosing is best for you.

WHICH TESTS AND PROCEDURES WILL BE PERFORMED DURING TREATMENT?

Every time you are seen in the clinic, your vital signs will be measured and you will be asked if you are experiencing any symptoms of your disease, other illnesses or side effects of treatment, and to provide the list of the medications you are taking.

The list of tests and procedures described below may be done a little earlier or later than the day indicated. The tests may also be done more frequently than indicated if your doctor feels it is necessary. If the screening tests are performed close to the first day of dosing, some of the tests listed below for Day 1 may not need to be repeated.

CYCLE 1

The following tests and procedures will be performed during Cycle 1.

Day 1:

- A physical exam including measurement of your vital signs and weight will be performed.
- You will be asked if you are experiencing any symptoms of your disease, other illnesses, or after start of treatment, side effects.
- You will be asked to give a list of all medications you are taking.
- Blood (about 3 teaspoons) will be collected for routine tests.
- Blood (about 2 teaspoons) will be drawn prior to sitravatinib dosing to measure biomarkers.

- You will have two sets of three ECGs performed before the pre-dose blood draws and one set 4 hours after sitravatinib dosing.
- Blood (about 1 teaspoon each time) will be drawn for sitravatinib pharmacokinetic (PK) testing within 30 minutes prior to dosing and again at about 30 minutes, 4 hours and 6 hours after dosing. PK testing is the measurement of the amount of sitravatinib in your blood.
- You will start your oral treatment with sitravatinib.
- You will receive your first infusion of nivolumab on study while at the clinic.

Day 15:

- A physical exam including measurement of your vital signs and weight will be performed.
- You will be asked if you are experiencing any symptoms or side effects.
- You will be asked to give a list of all medications you are taking.
- Blood (about 3 teaspoons) will be drawn for routine tests.
- You will have one set of three ECGs performed before the pre-dose blood draws.
- Blood (about 2 teaspoons) will be drawn prior to sitravatinib dosing to measure biomarkers.
- Blood (about 1 teaspoon) will be drawn prior to sitravatinib dosing for PK testing.
- You will continue your treatment regimen with sitravatinib and nivolumab.

CYCLE 2

The following tests and procedures will be performed during Cycle 2.

Day 1:

- A physical exam including measurement of your vital signs and weight will be performed.
- You will be asked if you are experiencing any symptoms or side effects.
- You will be asked to give a list of all medications you are taking.
- Blood (about 3 teaspoons) will be collected for routine tests.
- You will have one set of three ECGs performed prior to sitravatinib dosing.
- Blood (about 1 teaspoon) will be drawn prior to sitravatinib dosing for PK testing.
- If you agree, you will have a tumor biopsy taken to measure immune system markers that may change during study treatment.
- You will continue your treatment regimen with sitravatinib and nivolumab.

Day 15:

- A physical exam including measurement of your vital signs and weight will be performed.

- You will be asked if you are experiencing any symptoms or side effects.
- You will be asked to give a list of all medications you are taking.
- Blood (about 3 teaspoons) will be collected for routine tests.
- You will have one set of three ECGs performed before sitravatinib dosing.
- Blood (about 1 teaspoon) will be drawn prior to sitravatinib dosing for PK testing.
- You will continue your treatment regimen with sitravatinib and nivolumab.

CYCLE 3

The following tests and procedures will be performed during Cycle 3.

Day 1:

- A physical exam including measurement of your vital signs and weight will be performed.
- You will be asked if you are experiencing any symptoms or side effects.
- You will be asked to give a list of all medications you are taking.
- Blood (about 3 teaspoons) will be collected for routine tests.
- Blood (about 1 teaspoon) will be drawn prior to sitravatinib dosing for PK testing.
- You will have an echocardiogram performed
- You will have one set of three ECGs performed before sitravatinib dosing.
- You will continue your treatment regimen with sitravatinib and nivolumab.

Day 15:

If you are receiving your nivolumab administration every 4 weeks (Q4W) or have discontinued nivolumab (with continuation of sitravatinib) you will not need to come into the clinic for this visit.

- A physical exam including measurement of your vital signs and weight will be performed.
- You will be asked if you are experiencing any symptoms or side effects.
- You will be asked to give a list of all medications you are taking.
- Blood (about 3 teaspoons) will be collected for routine tests.
- You will continue your treatment regimen with sitravatinib and nivolumab.

CYCLE 4 AND LATER TREATMENT CYCLES

The following tests and procedures will be performed during Cycle 4 and each future treatment cycle.

Day 1:

- A physical exam including measurement of your vital signs and weight will be performed.
- You will be asked if you are experiencing any symptoms or side effects.
- You will be asked to give a list of all medications you are taking.
- Blood (about 3 teaspoons) will be drawn for routine tests.
- During Cycle 5 only, blood (about 1 teaspoon) will be drawn prior to sitravatinib dosing for PK testing.
- During Cycle 5 only, you will have one set of three ECGs performed before sitravatinib dosing.
- You will continue your treatment regimen with sitravatinib and nivolumab.

Day 15:

If you are receiving your nivolumab administration every 4 weeks (Q4W) or have discontinued nivolumab (with continuation of sitravatinib) you will not need to come into the clinic for Day 15 visits beyond Cycle 2 Day 15.

- A physical exam including measurement of your vital signs and weight will be performed.
- You will be asked if you are experiencing any symptoms or side effects.
- You will be asked to give a list of all medications you are taking.
- You will continue your treatment regimen with sitravatinib and nivolumab.

Assessment of your disease:

In addition, every 8 weeks you will have CT or MRI scans to measure the size of the tumor(s). Depending on where your tumors are located, a whole body bone scan may be performed or scans in addition to a CT scan may be used.

If your tumor responds well to treatment, at the time that you have CT or MRI scans performed to confirm the response (4-8 weeks after it is first observed) you will have a blood draw (about 4 teaspoons) to see whether the tumor response has changed the amount or kind of circulating tumor DNA.

At any time between Screening and the last day of treatment you may need to return to the clinic for additional evaluations if your doctor feels this is necessary to follow any side effects of treatment or symptoms of your disease more closely. If you experience a severe side effect of treatment, an unscheduled blood sample for PK assessment may be drawn.

COVID-19 Pandemic:

To keep you, the study doctor and their staff safe during the COVID-19 Pandemic, some of your visits **may** be conducted remotely by telephone/video conference or at your residence by a

qualified home health care professional, if such a service is available. The study doctor will discuss these options with you in detail if they are applicable. Let your study doctor know if you have any questions about visit requirements or options.

LENGTH OF STUDY

HOW LONG WILL I REMAIN ON THE STUDY?

You may remain on this study for as long as your disease doesn't get worse such that the doctor feels you should stop study treatment, and as long as you tolerate the drugs (the side effects are not severe), and you wish to continue.

Treatment with sitravatinib and nivolumab will be stopped if:

- your disease worsens such that the doctor feels treatment should be stopped;
- side effects are very severe;
- your doctor feels that this is no longer the best treatment for you;
- you choose to no longer participate;
- you do not comply with the study procedures (for example, if you do not take study medication, or do not return as instructed for clinic visits); or
- you become pregnant.

In addition, the study may be stopped early and at any time based on the decision of the sponsor (Mirati Therapeutics, Inc.), if deemed appropriate.

By signing this consent form, you are indicating your intention to cooperate with the study requirements. However, you may decide to stop treatment or stop your participation in this study at any time. Your care and your future care will not be affected by your decision to stop participating in this study. You should tell the study doctor if you are thinking about stopping or decide to stop participation in this study.

If you discontinue study treatment, your study doctor will explain other treatments available to you.

WHAT WILL HAPPEN AT THE END OF TREATMENT AND AFTER THAT?

At the time you stop treatment, the following tests and procedures will be performed unless they were performed recently:

- You will have a full physical exam, including measurement of your vital signs and weight.
- You will be asked if you are experiencing any symptoms or side effects.
- You will be asked to give a list of all medications you are taking.
- Blood (about 3 teaspoons) will be collected for routine tests.

- Blood (about 2 teaspoons) will be drawn to measure biomarkers.
- You will have an ECG performed.
- You will have an echocardiogram performed.
- You will have a blood draw (about 4 teaspoons) to see whether the tumor response has changed the amount or kind of circulating tumor DNA.
- If you agree, you will have a tumor biopsy taken to measure immune system markers that may change during study treatment.

In addition, the study staff will contact you at least 28 days after your last study treatment dose to see if you are having any continuing side effects. If you are experiencing serious side effects at that time, you will be asked to allow follow-up until the side effects resolve or return to normal.

You will also be contacted by the study staff by phone every 2 months after study participation to ask how you are doing and what new treatments you are receiving for your lung cancer.

If you end study treatment for reasons other than worsening of your disease, you will continue to have disease assessments performed until you start new treatment for your lung cancer or your disease worsens.

POTENTIAL RISKS, SIDE EFFECTS, AND DISCOMFORTS

While on this study, you are at risk for potential side effects (symptoms that may be related to your study treatment). These side effects will vary in people and are unpredictable. You should discuss these with the study doctor.

Sitravatinib

Among the side effects described in the most recent formal summary of experience (cut-off date 26 June 2021) with sitravatinib in 220 patients treated with sitravatinib alone, approximately 865 patients treated with sitravatinib in combination with either nivolumab or tislelizumab (a drug similar to nivolumab), 10 patients treated with sitravatinib in combination with nivolumab and ipilimumab (an immunotherapy), and 13 patients treated with sitravatinib in combination with pembrolizumab (a drug similar to nivolumab) and enfortumab vedotin (an antibody drug conjugate chemotherapy) the following were the most common side effects, either related to sitravatinib when given alone or when given in combination with one of the other drugs mentioned above:

Drug related side effects reported in ≥10% of the patients:

- Diarrhea
- Fatigue (tiredness)
- Nausea
- Increased blood pressure

- Vomiting
- Decreased appetite
- Changes in the skin of the hands and feet; redness, swelling, pain and/or formation of blisters (Hand and Foot Syndrome)
- Abnormal liver tests (may indicate possible liver damage)
- Weight loss
- Hoarse voice
- Inflamed and sore mouth
- Reduced thyroid function
- Protein in urine (which may indicate problems with the kidneys)

Drug-related side effects reported in ≥5% and <10% of the patients include:

- Increase in pancreatic enzymes (this could indicate damage to the pancreas due to injury, infection, or inflammation)
- Abdominal pain
- Dry mouth
- Skin rash
- Dizziness
- Decrease in red blood cells (anemia which may cause tiredness)
- Constipation
- Change in taste
- Decrease in platelets (cells that help form blood clots to stop bleeding)
- Increase in thyroid stimulating hormone (may indicate reduced thyroid function)
- Increase in alkaline phosphatase (may indicate liver damage or bone disorder)
- Low albumin (may indicate liver disease, kidney disease, malnutrition, infection, inflammation, or thyroid disease)

Less common (<5%) but significant drug-related side effects observed include:

- Decrease in the pumping of the heart
- Blood clots, including those involving the lung
- Very high blood pressure
- Inflammation of the pancreas
- Decrease in white blood cells (risk of infection) with development of fever

- Inflammation of the colon or skin (seen with sitravatinib given alone); and inflammation of the lungs, colon, skin, thyroid, or heart muscle (seen with sitravatinib given with nivolumab)
- Ischemic or hemorrhagic (bleeding) stroke
- Life-threatening bleeding
- Decreased sodium levels in the blood (which can manifest as loss of energy, nausea, vomiting, confusion and muscle spasms)
- Decreased potassium levels in the blood (which can manifest as severe muscle weakness)
- Increased potassium levels in the blood (which can manifest as muscle weakness, numbness, tingling, nausea, abdominal pain, diarrhea, chest pain, heart palpitations or arrhythmia)
- Acute kidney injury (which can cause fatigue, loss of appetite, confusion, nausea and vomiting)
- Electrocardiogram QT prolongation, effects on the electrical system of the heart, which might cause arrhythmias
- Life-threatening infection

Other less frequent (<1%) but significant adverse events that have been observed, include:

- Heart failure or stopping of the heart
- Heart attack
- Hepatic encephalopathy (decline in brain function due to severe liver damage)
- Life-threatening stomach ulcer perforation (hole)
- Life-threatening bowel ulcer
- A syndrome that can include headache, confusion, visual disturbances, and/or seizures, sometimes with stroke-like symptoms, typically occurring with hypertension (and known as posterior reversible encephalopathy syndrome [PRES] or reversible posterior leukoencephalopathy syndrome). These symptoms tend to resolve after a period of time, although visual changes sometimes remain

Based on what is commonly seen in patients receiving other cancer therapies from the same class of drug, additional side effects may occur on this study, including difficulty with wound healing.

Nivolumab (OPDIVO®)

The following information is provided in the most recent FDA approved Prescribing Information for OPDIVO. Your study doctor will inform you of any new OPDIVO risks.

What is the most important information I should know about OPDIVO?

OPDIVO is a medicine that may treat your melanoma, lung cancer, kidney cancer, blood cancer or head and neck cancer by working with your immune system. OPDIVO can cause your

immune system to attack normal organs and tissues in many areas of your body and can affect the way they work. These problems can sometimes become serious or life-threatening and can lead to death. These problems may happen anytime during treatment or even after your treatment has ended. **Call or see your study doctor right away if you develop any symptoms of the following problems or these symptoms get worse:**

Lung problems (pneumonitis). Symptoms of pneumonitis may include:

- new or worsening cough
- chest pain
- shortness of breath

Intestinal problems (colitis) that can lead to tears or holes in your intestine. Signs and symptoms of colitis may include:

- diarrhea (loose stools) or more bowel movements than usual
- blood in your stools or dark, tarry, sticky stools
- severe stomach-area (abdomen) pain or tenderness

Liver problems (hepatitis). Signs and symptoms of hepatitis may include:

- yellowing of your skin or the whites of your eyes
- dark urine (tea colored)
- severe nausea or vomiting
- bleeding or bruising more easily than normal
- pain on the right side of your stomach area (abdomen)
- feeling less hungry than usual
- drowsiness
- decreased energy

Hormone gland problems (especially the thyroid, pituitary, adrenal glands, and pancreas). Signs and symptoms that your hormone glands are not working properly may include:

- headaches that will not go away or unusual headaches
- hair loss
- extreme tiredness
- feeling cold
- weight gain or weight loss
- constipation
- dizziness or fainting
- voice gets deeper
- changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness
- excessive thirst or lots of urine

Kidney problems, including nephritis and kidney failure. Signs of kidney problems may include:

- decrease in the amount of urine
- blood in your urine
- swelling in your ankles
- loss of appetite

Skin Problems. Signs of these problems may include:

- rash
- itching
- skin blistering
- ulcers in mouth or other mucous membranes

Problems in other organs. Signs of these problems may include:

- changes in eyesight
- severe or persistent muscle or joint pains
- severe muscle weakness
- chest pain

Getting medical treatment right away may keep these problems from becoming more serious.

Your study doctor will check you for these problems during treatment with OPDIVO. Your study doctor may treat you with corticosteroid or hormone replacement medicines. Your study doctor may also need to delay or completely stop treatment with OPDIVO, if you have severe side effects.

What should I tell my study doctor before receiving OPDIVO?

Before you receive OPDIVO, tell your study doctor if you:

- have immune system problems such as Crohn's disease, ulcerative colitis, or lupus
- have had an organ transplant
- have lung or breathing problems
- have liver problems
- have any other medical conditions
- are pregnant or plan to become pregnant. OPDIVO can harm your unborn baby.
    - Females who are able to become pregnant should use an effective method of birth control during and for at least 5 months after the last dose of OPDIVO. Talk to your study doctor about birth control methods that you can use during this time.
    - Tell your study doctor right away if you become pregnant during treatment with OPDIVO.

- are breastfeeding or plan to breastfeed. It is not known if OPDIVO passes into your breast milk. Do not breastfeed during treatment with OPDIVO.

Tell your study doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Know the medicines you take. Keep a list of them to show your study doctor and pharmacist when you get a new medicine.

What are the possible side effects of OPDIVO?

OPDIVO can cause serious side effects, including:

See "What is the most important information I should know about OPDIVO?"

Severe infusion reactions. Tell your doctor or nurse right away if you get these symptoms during an infusion of OPDIVO:

- chills or shaking
- itching or rash
- flushing
- shortness of breath or wheezing
- dizziness
- fever
- feeling like passing out
- back or neck pain

Complications of stem cell transplant that uses donor stem cells (allogeneic). These complications can be severe and can lead to death. Your study doctor will monitor you for signs of complications if you have an allogeneic stem cell transplant.

The most common side effects of OPDIVO when used alone include:

- feeling tired
- pain in muscles, bones, and joints
- diarrhea
- weakness
- shortness of breath
- decreased appetite
- upper respiratory tract infection
- headache
- vomiting
- rash
- itchy skin
- nausea
- cough
- constipation
- back pain
- fever
- stomach area (abdominal) pain
- urinary tract infection

These are not all the possible side effects of OPDIVO. For more information, ask your study doctor.

Unexpected and possibly severe, life-threatening or fatal side effects could occur. This is the first time that sitravatinib will be given in combination with nivolumab, therefore, there may be side effects that have not been reported for either study drug when given alone. The study has

been designed to monitor closely for side effects, but unexpected side effects are possible. The long-term effects of sitravatinib and nivolumab are unknown.

If significant new side effects or information about your disease and sitravatinib and nivolumab are discovered during this study, you will be told.

This research study may involve unpredictable risks to the participants.

Other Risks

As with any new drug exposure, there is a risk of allergic reactions that can be fatal. These reactions usually start shortly after taking the drug. Symptoms may be skin itching and redness, difficulty breathing and/or low blood pressure and may be severe in some cases.

Tell your study doctor about any side effects you are experiencing and seek medical attention when necessary.

Other unknown side effects are possible.

Blood Draws

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count).

CT Scans and Bone Scans

You may feel some discomfort or anxiety when lying inside the CT scanner. A dye is injected and may cause you to get a metallic taste in your mouth, to feel warm and, rarely, experience nausea or vomiting. You will be exposed to a low amount of radiation used for the CT scan. If you are especially concerned with radiation exposure, you should discuss this with the study doctor.

MRI Scans

MRI examinations release radio waves, which are very noisy. Although radio and magnetic waves used in MRI examinations are not associated with any known side effects, long term effects still remain undetermined. You may experience brief claustrophobia (discomfort, fatigue or fear as a result of being in a small, enclosed space) during the MRI procedure. If this happens, you may be given medication to increase your comfort level or you may request to end participation in the MRI procedure. There are no known effects from exposure to the magnetic fields.

ECG

The risks during ECGs can include skin irritation and a rash due to wearing and the removal of the electrodes. The electrodes only detect electrical impulses produced by the heart. No

electricity passes through the body from the machine, and there is no danger of getting an electrical shock.

Tumor Biopsies

The risks of tumor biopsy include possible pain, discomfort, bleeding, swelling, scarring, bruising and infection, which can be life-threatening or fatal in rare cases. To reduce these risks, the site of the biopsy will be numbed and sterile techniques will be used. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site. There may be additional side effects, including severe side effects, depending on the location of your biopsy. Your doctor will discuss with you the safest method and location to perform this biopsy.

Pregnancy-Related Risks

Nivolumab (OPDIVO) can harm an unborn baby. It is not known if treatment with sitravatinib will also harm an unborn or breastfeeding baby. Women enrolled in the study (or your female partner if you are male) should not become pregnant or breastfeed a baby during the study and for 6 months after treatment completion. If you are a pregnant woman, you will not be enrolled in this study.

If women enrolled in the study (or your female partner if you are a male enrolled in the study) become pregnant during the study, you must tell your study doctor right away. The Sponsor may ask for access to both the mother and the infant's medical records for a minimum of 3 months after delivery. Should that need arise, written consent will be requested to provide such information.

If you are a woman of childbearing potential or if you are a man with a partner of childbearing potential, you and/or your partner must use an effective form of birth control approved by the study doctor during the clinical study and until 6 months after the last dose of study drug, or be in a situation, in the opinion of the doctor, not requiring birth control (such as being post menopausal for more than 1 year or effective surgical sterilization).

Examples of effective surgical sterilization include bilateral tubal ligation sterilization at least 6 months before the screening visit, hysteroscopic sterilization (e.g., ESSURE or ADIANA procedure) with confirmation test (hysterosalpingogram) at least 6 months before the screening visit, or a vasectomy at least 6 months before the screening visit.

Therapies to be Avoided During Participation in Study

The following treatments to be avoided during the study:

- Other anti-cancer treatment including chemotherapy and radiotherapy.
- Other investigational (experimental) therapy.
- Herbal medications and preparations.
- Medications that are processed by liver enzymes, your doctor will council you on these.

- Medications known to have risk of changing the electrical activity in the heart.
- Medications that suppress or reduce the strength of the body's own immune system. Some of these types of medications may be allowed to treat your symptoms or other medical conditions. Your doctor will council you on these.
- Vaccines against certain viruses like measles, mumps, and chickenpox. Some types of vaccinations, such as the flu vaccine, are permitted. Your doctor will council you on these.

Other medications should only be used with caution because sitravatinib in combination with nivolumab may alter the way these drugs work. Your doctor will review all medications you are taking.

NEW INFORMATION

During the study, you will be informed of any relevant new information on the study drugs sitravatinib and nivolumab.

ALTERNATE PROCEDURES OR TREATMENTS

You may choose not to take part in this study and discuss other treatment options and their related benefits and risks with your study doctor. Alternatives include participation in a different clinical trial to receive an experimental drug or treatment with available cancer treatments different than those you have already received. Your study doctor will give you more information about the best alternative for you.

COSTS

The study sponsor will provide sitravatinib free of charge for your use in this study. You or your insurance provider or health plan will be responsible for all costs related to your medical care not covered as part of this study.

Any tests or procedures that are being done solely for the purpose of this research study will be performed free of charge to you.

You might have unexpected expenses from being in this research study. These charges may be submitted to your health insurance. However, your health insurance may not pay these charges because you are in a research study. Ask the study doctor to discuss the costs that will or will not be covered by the sponsor.

PAYMENT FOR PARTICIPATION

You will not receive payment for participation in this study.

COMPENSATION FOR INJURY

If, during the course of the study, you experience any injury as a direct result of taking part in this study, proper care will be provided to you and your insurance provider or health plan will be billed for the cost of treatment. Your insurance or health plan provider may or may not pay for treatment of injuries as a result of your participation in this study. If you have concerns about your insurance coverage, you may want to contact your insurance or health plan provider.

There is no plan to provide any financial compensation for such injury except for what may be provided through remedies available to you under the law. No money is available from the institution where you are being treated or from the sponsor of this study as compensation for research-related injury. You will be asked to cooperate in obtaining any proceeds from insurance or other party coverage that may be available to you for such medical care.

You do not waive any of your legal rights by signing this form.

VOLUNTARY PARTICIPATION/WITHDRAWAL

Make sure that your study doctor has answered your questions. You can ask your study doctor questions at any time in the future.

Taking part in this study is voluntary. You can refuse to take part right now or can stop taking part at any time. Deciding not to take part or deciding to leave the study later will not result in any penalty or any loss of benefits to which you are entitled.

Your participation in this study may be stopped at any time by the study doctor or the sponsor without your consent for any of the following reasons:

- if it is in your best interest;
- you do not consent to continue in the study after being told of changes in the research that may affect you;
- you do not continue to meet the study requirements; or
- for any other reason.

You will be given a copy of this signed and dated consent form.

In no way does signing this consent form waive your legal rights nor does it relieve the study doctor(s), sponsor(s) or involved institutions from their legal and professional responsibilities.

SOURCE OF FUNDING FOR THE STUDY

Funding for this research study will be provided by Mirati Therapeutics, Inc.

POTENTIAL BENEFITS

You may have an improvement in your disease from the study treatment; however this cannot be guaranteed. Your condition may stay the same or get worse. We hope the information learned from the study will benefit other people with your condition in the future.

AUTHORIZATION FOR USE AND DISCLOSURE OF PROTECTED HEALTH INFORMATION

During the course of this study, your study doctor and the study staff at *[insert site name]* will be collecting information about you that they may share with certain individuals. Medical/study records that identify you, and the consent form signed by you, may be inspected by:

- The study sponsor and any authorized representative including study monitors and auditors who verify the accuracy of the study information, individuals with medical backgrounds who determine the effect that the study drugs have on the disease and who monitor the safety of the study drugs, and/or individuals who put all the study information together in report form;
- The United States of America Food and Drug Administration (FDA);
- Governmental agencies in other countries where the study drug is being used or considered for approval; and
- [*insert IRB name*]

This information may include your medical history, treatment schedule, and the results of any of your tests, therapies, or procedures. The purpose of collecting this information is to learn about how the study drugs affect your disease and any side effects you may experience as a result of your treatment.

Because of the need to release information to the parties mentioned above, absolute confidentiality cannot be guaranteed. The results of this study may be presented at meetings or in publications. However, your identity will not be disclosed in those presentations. All reasonable steps will be taken to ensure confidentiality.

You have the right to see and reproduce your medical/study records related to the research study for as long as this information is held by the study doctor. However, in some studies, in order to ensure the scientific value of the study, patients are not able to view or reproduce their medical/study records until the research has been completed with all participants in the study. If possible for this study, your study doctor will be able to discuss your clinical test results with you.

There is no expiration date for the use of this information as stated in this authorization. You may withdraw your authorization to share your personal health information at any time in writing. Contact the study staff for specific instructions on how to do this. If you withdraw your authorization, you will be removed from the study, and the study doctor and study staff will no longer use or disclose your personal health information in connection with this study, unless they need to use or disclose some of your research-related personal health information to preserve the

scientific value of the study. *[insert study site name]* and/or the study sponsor may continue to use any study data that were collected before you canceled your authorization.

If you refuse to provide your authorization to disclose your protected health information, you will not be able to participate in this research study.

Your personal health information will be protected according to state and federal law. All reasonable steps will be taken to ensure confidentiality.

CONTACT INFORMATION FOR QUESTIONS OR PROBLEMS

If you have questions about taking part in this study, if at any time you feel you have suffered a research-related injury or a reaction to the study drug, or if you have questions, concerns, or complaints about the research, you can ask your study doctor, *[insert name, phone numbers, hours available – should be a 24 hr number]*.

If you have questions about your rights as a research patient or if you have questions, concerns or complaints about the research, you may contact:

[insert IRB name, address, contact numbers]

[insert IRB name] is a group of people who perform independent review of research.

[insert IRB name] will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact *[insert IRB name]* if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

CONSENT/AUTHORIZATION FOR TUMOR SAMPLE AND BLOOD COLLECTION AND TESTING

1. You are being asked to give permission to use samples of your tumor to test for PD-L1 signal molecule expression and immune system markers. Testing of PD-L1 expression is required for patients who have not previously been treated with a checkpoint inhibitor. This is optional for patients who have been previously treated with a checkpoint inhibitor.

   I elect to ____ or not to ____ have tumor samples tested.

   Patient's Initials _____

2. You are being asked to have one or more biopsies of your tumor during the study if your doctor thinks that a biopsy can be performed with only reasonable risks. Having these biopsies is optional and will not determine whether you can participate in the study. If you indicate now that you are willing to have these biopsies, you have the right to later change your mind and not have the biopsies taken.

   I elect to ____ or not to ____ have one or more biopsies of my tumor taken while participating in the study. Patient's Initials _____

3. You are being asked to give permission to use samples of your blood to test for tumor genes. The testing will be done during screening and at several time points during study treatment.

   I elect to ____ or not to ____ have blood samples used for to test for tumor genes.

   Patient's Initials _____

4. You are being asked to give permission to collect previous test results about tumor PD-L1 expression or tumor genes in the blood or tumor tissue.

   I elect to ____ or not to ____ allow collection of results from previous tests performed.

   Patient's Initials _____

CONSENT/AUTHORIZATION

I have read the information in the consent form (or it has been read to me). I have had the chance to ask questions about this study and reflect and consult with others as needed. I agree to participate in this study. By signing this consent form, I am not giving up any of my legal rights. I have been given a copy of this consent form.

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above.

_____

PRINTED NAME OF PATIENT

_____ _____

SIGNATURE OF PATIENT DATE

---------- Use this legal representative section only if applicable ----------

I confirm that the information in the consent form and any other written information was accurately explained to the extent compatible with the patient's understanding. The patient freely consented to be in the research study.

_____

PRINTED NAME OF LEGAL REPRESENTATIVE

_____ _____

SIGNATURE OF LEGAL REPRESENTATIVE DATE

_____

Authority of Patient's Legally Authorized Representative or Relationship to Patient

---------- Use this witness section only if applicable ----------

If this consent form is read to the patient because the patient is unable to read the form, an impartial witness not affiliated with the research or study team must be present for the consent and sign the following statement:

I confirm that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the patient. The patient freely consented to be in the research study.

SIGNATURE OF IMPARTIAL WITNESS	DATE

Note: This signature block cannot be used for translations into another language. A translated consent form is necessary for enrolling patients who do not speak English.

ATTESTATION STATEMENT

I confirm that the research study was thoroughly explained to the patient. I reviewed the consent form with the patient and answered the patient's questions. The patient appeared to have understood the information and was able to answer the following questions correctly:

1. What is the purpose of this study?
2. If you decide to be in the study, what will you be asked to do?
3. What is the possible benefit of participating in this study?
4. What are the possible risks of participating in this study?
5. If you decide not to participate in this study, what options do you have?
6. Will participating in this study cost you anything? If so, what will you have to pay for?
7. Do you have to be in this study?
8. If you decide to be in the study, can you leave the study when you want to?

Printed Name of Person Conducting the Informed Consent Discussion	Date
Signature of Person Conducting the Informed Consent Discussion	Date

Signature Page for V15 VV-CLIN-000933

Approval	Lisa Latven Director, Clinical Operations Clinical Science Approved 24-Oct-2021 21:36:32 GMT+0000

Approval	Ronald Shazer Executive Medical Director Clinical Development Approved 25-Oct-2021 19:26:54 GMT+0000

Signature Page for V15 VV-CLIN-000933