UNIVERSITY OF MICHIGAN
CONSENT TO BE PART OF A RESEARCH STUDY

1. KEY INFORMATION ABOUT THE RESEARCHERS AND THE STUDY

Study title: A Phase 1, Open-Label, Dose-Escalation, and Dose-Expansion Study to Investigate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Efficacy of SRK-181 Administered Alone or in Combination with a Checkpoint Inhibitor in Patients with Locally Advanced or Metastatic Solid Tumors (DRAGON)

Company or agency sponsoring the study: Scholar Rock, Inc.

Name, degrees, and affiliations of the principal investigator:
Ulka Vaishampayan, MBBS Department of Internal Medicine; Hematology/Oncology; University of Michigan

More information about this study continues in Section 2 of this document.

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

This study involves the evaluation of investigational drug SRK-181, which is an anti-latent TGFβ1 monoclonal antibody. "Investigational" means that Study Drug is currently being tested and is not approved for use by regulatory authorities, such as the United States Food and Drug Administration (FDA). This is a new drug designed to be a potential anti-cancer therapy. SRK-181 is designed to be given by IV infusion every three weeks. The purpose of this study is to evaluate the safety, effectiveness and tolerability of SRK-181 in combination with anti-PD-(L)1 antibody therapy.

How does SRK-181 alone or SRK-181 in combination with an anti-PD-(L)1 antibody therapy work?

SRK-181 has been tested for safety in pre-clinical studies, which includes testing in animals, but this is the first study where it will be given to humans. We do not know if the study intervention will work the same way in humans as it has worked in pre-clinical studies. This type of study, which is a first study in humans, is called a phase 1 clinical study. Please talk with your study doctor to discuss the latest information about human results of SRK-181 alone or in combination with anti-PD-(L)1 therapies.

Anti-PD-(L)1 antibody therapy works by helping the immune system attack and kill cancer cells. But in many cases, anti-PD-(L)1 antibody therapy does not work, sometimes because the immune cells cannot get into the tumors or because the tumor has an environment in which the immune system is not able to be effective. A molecule called TGFβ may possibly play a role in some cases of anti-PD-(L)1 antibody therapy not working in tumors. This clinical study will test whether or not SRK-181 in combination with anti-PD-(L)1 antibody therapy can help the immune system attack and kill tumors.

The study is for the therapy of either locally advanced or metastatic solid tumors such as non-small cell lung cancer (NSCLC), urothelial carcinoma (UC), cutaneous melanoma (MEL), clear cell renal cell carcinoma (ccRCC) and head and neck squamous cell carcinoma (HNSCC).

Researchers want to find out if SRK-181 alone and/or in combination with Pembrolizumab can help people with cancer.

The purpose of this study is to find out:

- How much of SRK-181 or SRK-181 plus anti-PD-(L)1 antibody therapy is safe and tolerable to you
- What effects, good or bad, the study drug has on you and your health
- How much of SRK-181 gets into your bloodstream and how long it takes for your body to get rid of it (pharmacokinetic studies)
- How the study drug affects cancer cells and other types of cells (pharmacodynamic studies)
- If certain characteristics of cancers predict a better result with SRK-181 (predictive biomarkers)

There are 3 main parts to this study (A1, A2 and B). Part A1 and Part A2 have finished enrollment and no other patients will be enrolled into these parts of the study. Both Part A1 and Part A2 involve dose escalation. Part B involves dose expansion.

The University of Michigan will participate in Part B. The remainder of this document describes only this part.

You will be assigned to a study group that receives Pembrolizumab in combination with the study drug SRK-181. Use of Pembrolizumab in combination with SRK-181 is considered investigational (experimental). For this study, you will receive a dose of Pembrolizumab for patients with cancer. Pembrolizumab is an anti-cancer drug which has been approved by the U.S. Food and Drug Administration (FDA), for the treatment of specific types of cancer including NSCLC, UC, MEL, ccRCC, and HNSCC.. Use of Pembrolizumab for other types of cancer is considered investigational (experimental). For this study, you will receive a dose of Pembrolizumab, according to the label of the drug, for patients with cancer.

3. WHO MAY PARTICIPATE IN THE STUDY

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

You are invited to take part in a clinical study because you have been diagnosed with a solid tumor (cancer), that is not responsive to approved treatments or no currently approved therapy is available or is not tolerated by you or for which you have been evaluated by the study doctor as an unsuitable candidate for currently approved treatments.

Every study has strict guidelines for determining which people may participate. These are called eligibility criteria. You will need to meet all of these criteria before you can participate in this study. If you agree to consider participating in this study, you will undergo evaluations to see if you meet the eligibility criteria for this study. Even though you may meet all the criteria for participation, it is possible that you may not be enrolled in this study for other reasons.

3.2 How many people are expected to take part in this study?

It is planned that up to 254 people with cancers will participate in this study in approximately 20 medical centers across the United States and up to 6 sites in South Korea. Approximately 66 to 160 people will participate in Part B of this study. Approximately 5 subjects are expected to enroll in this study at the University of Michigan.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

The study team will explain the research study and answer any questions you have about the study. If you still want to participate in the study, the study team will request you sign the consent form prior to any activities occurring that pertain to the study. Once your consent is obtained, the study team will look through your medical chart, ask you questions, and begin scheduling tests and procedures to determine if you are eligible for the study. The study team will inform you of the types of tests and procedures required before the study begins.

Once it is determined you are eligible to enter the study, tests and procedures done at your study visits as part of your regular cancer care will continue, but some may be done more often because you are participating in this research study. Also, some of the tests or procedures may have to be repeated if, for example, they were done too long ago or the results are not normal.

Some tests and procedures may be done that are not part of your regular cancer care and are being done only for this research study. Tests and procedures that are performed more often or are not part of your standard cancer care will be identified below as “Research”.

How do I know if I can be in this study?

The first part of the study is called a screening period, which can last up to 28 days (about 4 weeks). During this time, the study doctor will decide if you qualify to be in the study. Many of your health factors will be considered including:

- You must be an adult age 18 or greater with a solid tumor which has been confirmed by laboratory testing and your doctor will determine if your tumor type is eligible for therapy on this study.
- Your study doctor will review your laboratory values, heart status, medical and surgical health history, allergies, current or recent medications and vaccines, unfavorable side effects of your current medications and recent, current or planned upcoming treatments to see if these are allowed in the study and if it is safe for you to join the study.
- You must have locally advanced or metastatic solid cancer.
- For some study participants, there is no current standard of care therapy options to treat your cancer. For some study participants, standard of care therapy may exist, but it may have failed in you or is not tolerated by you or you are not a suitable candidate and are not eligible for the usual standard of care therapy.

Certain types of cancers that are locally advanced or metastatic may have standard of care treatment options available to you. You may be eligible for such a therapy outside of this study and it may have a known benefit, including living longer. You and your study doctor should discuss this and confirm there are no other treatment options available to you (this may be because other options have failed, you do not tolerate them or for various reasons, you are not a good candidate for these treatments).

Your decision to participate in this study will mean you cannot participate in other clinical research studies or receive other treatments for your cancer, which otherwise could have been beneficial to you. Before enrolling in this study, it is therefore important to confirm with your study doctor that you are not eligible for other therapies that might be effective in treating your cancer. You should not participate if standard of care therapies could be an option for you.

The study has several parts, and your study doctor will review your medical history to determine whether you qualify for any of the study groups. In addition, there are special considerations related to anti-PD-(L)1 antibody therapy that you may have already received:

If you are being considered for Part B, in which subjects will be given both Pembrolizumab and SRK-181. You may not participate in this study if you never received anti-PD-(L)1 antibody therapy. You may participate in this study if you did not experience a treatment response to the anti-PD-1 antibody therapy. If you are enrolled in this study, you will receive study intervention with SRK-181 and pembrolizumab.

What will happen during this study?

You will be given SRK-181 in combination with Pembrolizumab. Study intervention will be given through your vein by an IV catheter. You will be connected to a machine called an infusion or syringe pump for the entire time when the study intervention is being given.

For the first two times you receive SRK-181, it will be given over 2 hours. There will be a 1-hour observation period after the infusion of SRK-181 finishes and before infusion of Pembrolizumab begins. Pembrolizumab can be given by IV infusion, over 30 minutes (or according to the product packaging instructions). You may have blood drawn 1 and 6 hours after completion of the drug(s) infusion. The third time you receive SRK-181, the SRK-181 IV infusion may be given faster than 2 hours. Not everyone can receive SRK-181 faster than two hours by IV infusion. Your study doctor will determine whether you are eligible and will let you know.

Subject Responsibilities:
Follow the study instructions, come to the study center for all visits with the study doctor/study staff or inform the team in advance if you cannot attend an appointment. Tell the study doctor or study staff about unfavorable changes in your health, changes in your prescribed or non-prescribed medicines, and if you want to stop being in the study.

The exact study intervention combination depends on which study group(s) you are assigned to.

In Part B, 5 study groups will be enrolled. . Based upon data from Parts A1 and A2, a recommended dose was selected, which is 1500 mg every 3 weeks. This is the dose that will be used for each study group in Part B. Testing at the recommended dose will evaluate how SRK-181 in combination with Pembrolizumab works on your cancer. Depending on your type of cancer and your eligibility, you may be enrolled into one of the following study groups:

- **Group Non-small cell lung cancer (NSCLC): Subjects with NSCLC** will receive SRK-181 plus Pembrolizumabgiven every 3 weeks with a fixed dose of 200 mg.

- **Group Urothelial carcinoma (UC): Subjects with UC** will receive SRK-181 plus Pembrolizumab given every 3 weeks with a fixed dose of 200 mg.

- **Group Cutaneous melanoma (MEL): Subjects with MEL** will receive SRK-181 plus Pembrolizumabgiven every 3 weeks with a fixed dose of 200 mg.

- **Group Clear cell renal cell carcinoma (ccRCC):** Subjects with ccRCC will receive SRK-181 plus Pembrolizumab given every 3 weeks with a fixed dose of 200 mg.

OR

- **Group** head and neck squamous cell carcinoma **(HNSCC): Subjects** will receive SRK-181 plus Pembrolizumab, given every 3 weeks with a fixed dose of 200mg.

Part B of the study may be expanded to include additional tumor types and/or additional immunotherapy combinations based on emerging study information.

Your study doctor will tell you whether you qualify for Part B.

<u>What happens when I come for study visits for study procedures?</u>
Your regular medical care includes tests and procedures. Before you can start the study, the study doctor or a member of the study staff can answer any questions you may have about which tests and procedures are part of

the study and are not part of your regular medical care. You will need to sign this form if you want to be in the study and before the study doctor or study staff can begin the screening period to see if you qualify for the study. You will have some exams, tests, and procedures for this study. If you have had some of these tests recently, they may not need to be done again. This will be up to your study doctor. At every study visit, you will be asked about your overall health status, whether you are experiencing anything unusual or if you are having any reactions to the study intervention. You will be asked about any new medications or treatments.

There will be several types of blood tests that will be done at specific times. The following provides a description of the blood tests:

Pharmacokinetics (PK) Studies
Pharmacokinetics (PK) refers to what the body does to a drug and determines the movement of the drug into, through and out of the body. Blood samples are taken at specific times to measure how much of the study drug is in the blood at different times after the drug was administered. This is needed to gain an understanding of when the effect of the drug starts, how long it lasts, and how strong the effect is.

Pharmacodynamic (PD) Studies
Pharmacodynamic studies refer to tests to see the effect of a drug on the body and your cancer. This study includes tests to measure how long study drug is attached to your immune cells after each dose, and to measure the effect of study drug on immune cells in your blood and in biopsies of your cancer. This will help researchers to understand how SRK-181 works and help to determine the best dose of SRK-181.

Predictive Biomarkers (PB) Studies
Sometimes test results called predictive biomarkers can help predict which subjects are most likely to benefit from a specific treatment. Several tests are being done as part of this study to see if subjects whose cancers have certain characteristics are more likely to benefit from SRK-181. These tests include tests on blood samples and tumor biopsies to look for certain markers and gene patterns.

Correlative (CS) Studies
Correlative studies see how a person's genes (by RNA level) and presence of immune cells within the tumor and in circulation affect response to a drug and how SRK-181 could change these responses. Tests will be done in tumor and in blood samples before and after study intervention to compare these measurements. This will enable scientists to understand these effects and potentially help identify ways to detect the effects of SRK-181 in subjects in the future.

Safety Studies
Safety studies will be done by taking a blood sample from your vein to check on your health status. The tests include hematology, chemistry, coagulation, thyroid studies and cytokine studies to help evaluate your health status and help see if there are any harmful effects the study intervention may be causing.

Pregnancy Test: A pregnancy test will be done for any participant of child-bearing potential. This will be done before every study intervention administration during the study. The study doctor or study staff will tell you if the pregnancy test results are positive. The results of the pregnancy testing must be negative for you to be in the study.

Anti-Drug Antibodies (ADA): The body can potentially develop antibodies against the study drug. These are called anti-drug antibodies (ADA). These could limit the way the study drug works or even cause allergic reactions that in some cases may be life-threatening. You will have blood tests drawn to check for ADA during the study.

Screening Visit: (All Participants) After you sign this form, the following activities will occur:

- **Demographic questions:** You will be asked to provide personal information, such as your name, date of birth, age, race, and gender.
- **Health and medication questions including functional status:** You will be asked to answer questions about your health, your medical history, your cancer history and the medications you take, as well as questions about your general well-being and activities of daily life.
- **A physical exam** to review your body systems as well as your height and weight.
- **Vital signs** including your blood pressure, your heart rate, breathing and temperature.
- **Blood samples for safety** (about 5 teaspoons). This is for research.
- **Urine sample to test for possible pregnancy** if you are a woman of child-bearing potential. This is for research.
- **Urine sample** for analysis. This is for research.
- **Electrocardiogram:** An electrocardiogram (ECG) measures the electrical activity of your heart and is done up to 28 days (about 4 weeks) before you receive your first study intervention of study drug. This is for research.
- **Transthoracic echocardiogram:** A test to look at the structure and function of your heart. A lubricant clear jelly is placed on your chest and a wand scanner uses the jelly to slide over the area where your heart is located to see how your heart is working. This is for research.
- **Fresh tumor tissue:** A tumor sample, also called a biopsy, will be taken for testing to see if SRK-181 is having the expected effect on the tumor immune cells. In Part B, you will have a tumor biopsy before starting study intervention and 28-48 days after starting treatment. Tumor samples will also be tested for exploratory research on biomarkers to see if they predict a better tumor response (PB) and provide baseline measurements for correlative studies. This is for research.
- **Positron emission tomography (PET) Scans** looks at what happens after radioactive glucose is given through the vein and a scanner is used to explore the possibility of cancer spreading to other body locations. Because of the amount of radiation you are exposed to is small, the risk of negative effects from it is low. But the tracer might cause a major allergic reaction, in rare instances. Computed Tomography (CT) Scan of the thorax, abdomen and pelvis – from the neck down to the groin) is done to evaluate the status of your tumor. A CT scan uses a small amount of radiation (X-rays) to make pictures of body tissue and structures. For this test, you may receive contrast dye, by mouth and/or in a vein with a needle. The study doctor or study staff can tell you more about contrast dye.
- **Magnetic Resonance Imaging (MRI)** (or powerful magnets and radio waves, scan and evaluate the status of your tumor and make pictures of body tissue and structures. During an MRI, you must lie on your back in the MRI scanner without moving. The inside of the MRI scanner is a tight space. You may receive a contrast dye by mouth and/or in a vein with a needle. The study doctor or study staff can tell you more about the contrast dye and you may receive instructions on how to take any additional medication required. This may be the best scan to evaluate the status of your tumor instead of a CT scan. Your study doctor will decide whether a CT or an MRI is the best scan for your tumor. You will have a brain scan if there is a possibility you have a nervous system tumor.

Study Procedures Information

- **The following tests and procedures will be done at all study visits**
    - You will be asked about all medications you are currently taking.
    - You will be asked about any symptoms you are experiencing.
    - Physical exam, including weight.
    - Vital signs

- Evaluation of your functional status / activities of daily living
- Blood samples (about 3-4 teaspoons) for routine safety tests except Day 8.
- Urine sample for routine safety tests except Day 8.
-

- **The following tests and procedures will be done on Day 1 of every Cycle**
  - Urine sample for possible pregnancy before every infusion. This is for research.
  - Study Treatment: Infusion of SRK-181 in combination with Pembrolizumab.
  - **You are required to wait in the clinic** for an observation period of at least 4 hours after the first 3 SRK-181 infusions and if the study doctor thinks it is safe to do so, your wait period can be shortened to 2 hours after the SRK-181 infusion for the rest of the infusions.

- **The following tests and procedures will be done at specific intervals**
  - CT Scan (thorax, abdominal and pelvis) or MRI Scan to see how your disease is doing 6 weeks (about every 1 and a half months) after your first treatment and approximately every 9 weeks (about 2 months) for the next 6 months of treatment and every 12 weeks (about 3 months) thereafter.
  - A required biopsy will be taken between Day 28- 48. The biopsy is taken to see if SRK-181 is having the expected effect on the tumor immune cells. This is for research.
  - Transthoracic echocardiogram will be performed on Day 1 of Cycle 2 and Cycle 3, and then about every 12 weeks (about 3 months) from Cycle 3 Day 1 until treatment week 48 and then every 24 weeks (about 5 and a half months) thereafter. This is for research.

Additional Study Procedures for each Visit

You are participating in Part B of the Study, during study cycles 1-3, you will be asked to come into the clinic on Days 1, Day 8 and Day 15. You will be asked to come in on Day 1 for cycles 4-through 9. If you continue into the Long-Term Extension Phase, you will come in on Day 1 of every cycle. Blood samples, ECG, Echocardiogram, and urine samples listed below are for research.

Cycle 1, Day 1

- Blood sample (about 5 teaspoons) for research tests before infusion
- Blood sample (about 3 teaspoons) for research tests 1 hour after infusions
- ECG before and 1 hour after infusion

Cycle 1 Day 8

- Blood sample (about 2 teaspoons) for research tests

Cycle 1, Day 15 (for every 3-week participants)

- Blood sample (about 1 teaspoon) for research tests

Cycle 2 Day 1

- Blood sample (about 5 teaspoons) for research tests before infusion
- Blood sample (about 2 teaspoons) for research tests 1 hour after infusion
- ECG before infusion
- Transthoracic Echocardiogram before infusion

Cycle 3 Day 1

- ECG before and 1 hour after infusion
- Blood samples (about 5 teaspoons) for research tests before infusion
- Blood samples (about 3 teaspoons) for research tests 1 hour after infusion

- Transthoracic echocardiogram before infusion (this assessment will then be repeated every 12 weeks for the first 48 weeks during the study and then repeated once every 24 weeks moving forward).

Cycle 3 Day 8

- Blood sample (about 3 teaspoons) for research tests

Cycle 4 Day 1

- Blood sample (about 5 teaspoons) for research tests before infusion
- Blood sample (about 2 teaspoons) for research tests 1 hour after the infusion
- ECG before infusion

Cycle 5 Day 1

- Blood Sample (about 4 teaspoons) for research tests before infusion
- Blood Sample (about 2 teaspoons) for research tests 1 hour after infusion
- ECG before and 1 hour after infusion

Cycle 6 Day 1

- Blood sample (about 4 teaspoons) for research tests before infusion
- Blood sample (about 2 teaspoons) for research tests 1 hour after the infusion

Cycle 7 Day 1

- Blood sample (about 4 teaspoons) for research tests before infusion
- ECG before infusion

Day 1 of Cycle 9 and Beyond (Cycle 10 Day 1 infusion starts the Long-Term Extension Phase)

- Blood samples (about 5 teaspoons) for research tests (cycles 9, 12, 16, 24, 30) before infusion
- ECG before infusion on odd cycles

Final Visit – End of Study Intervention 4 weeks after the last dose of study drug:

- ECG
- Urine sample to test for possible pregnancy
- Blood samples (about 4 teaspoons) for research tests
- Transthoracic Echocardiogram
- Imaging is not required on this visit if done within the prior 4 weeks.

Unscheduled Visits

For your safety, your doctor may request that some tests be repeated at time points not listed here.

Survival Follow Up

If you stop taking the study drug(s), the study staff will call you to check on how you are doing and any new anti-cancer treatments you have started, every 3 months for up to 3 years. This phone call should take about 5-10 minutes.

Early Termination

If your study treatment stops early, you will have an Early Termination (ET) visit. You will need to return to the study site 4 weeks after your last dose of study drug for the final visit.

What will happen to my collected samples?

The study involves the collection of biologic samples including blood, urine and tissue. Your samples will be shipped to an accredited central laboratory selected by the Sponsor that will store and analyze your samples. Your samples will be stored for 2 years after the last marketing application approval, or if not approved 2 years following the discontinuance of the test article for investigation. Your tumor tissue samples may be shipped to additional specialty laboratories that will analyze how your cancer responds to the study procedures.

4.2 How much of my time will be needed to take part in this study?

The length of your study visits will vary depending on which procedures need to be done.

- The screening visit may take approximately 8-10 hours, (however not all of the tests and procedures need to be done on the same day).
- Visits during the study intervention period may take approximately 2-4 hours.
  - On days when you receive the study drug infusion, those visits may take 2-4 hours longer.
  - On some days when blood samples will be collected to measure the amount of study drug in your blood, those visits may take 8-10 hours.
  - On days when you have a biopsy or imaging scans, those visits may take 1-2 hours longer.
- End of Study Intervention visit may take approximately 2-4 hours.
- Survival Follow-up visits may take approximately 5-10 minutes *and* will be done over the phone, every 3 months for up to 3 years.

4.3 When will my participation in the study be over?

The amount of time you will be treated with the study intervention is determined by the study group to which you are assigned. Everyone in the study has a screening period that lasts up to 28 days. A cycle begins with the day you receive study intervention, which is then given every 21 days. The 21-day interval (for every 3-week cycle) begins with the study intervention day (the day you receive the study medication). This is called a “cycle”.

After the screening period, you will be assigned to one of the Part B Groups:
9 treatment cycles lasting 21 days/cycle (about 3 weeks). If after 9 cycles you continue treatment, you will be entered into the Long-Term Extension Phase (LTEP). You will have less assessments (e.g. lab tests, etc) in LTEP than in the initial 9 treatment cycles. Your study doctor will continue to evaluate you for the effectiveness and safety of the Study Drug treatment during the LTEP.

Treatment during the LTEP may continue for up to 2 years from the start of study intervention, as long as you have clinical benefit in the opinion of the study doctor and show no signs or symptoms of disease progression, unacceptable toxicity, or have other reasons for study discontinuation.

Continuation of study therapy beyond 2 years must be approved by the Sponsor based on the safety of SRK-181 and will depend on the continued availability of SRK-181.

Your participation in the study may be stopped if your cancer progresses, you have unacceptable side events from the Study Drug, or you meet any other criteria for withdrawal from the study. Your continuation of SRK-181 depends on the Sponsor, study doctor, and the continued availability of SRK-181.

You can stop receiving study intervention and stop participating in this study at any time during the study and you will be asked to have an End of Study Visit 4 weeks after the final study intervention dose is given to you.
You will be followed by your study team to see how you are doing (via telephone contact every 3 months) for up to 3 years.

4.4 What will happen with my information and/or biospecimens used in this study?
The information that follows applies to information and/or specimens collected and/or used in both the main study and the sub-study, as well as to unspecified future use of your information and/or samples. Your collected information and biospecimens will be shared with the sponsor, Scholar Rocks, Inc.

Your collected information and biospecimens may also be shared with other researchers, both here or around the world, or with companies. Any sharing is subject to contractual obligations with the Sponsor. Additionally:

- With appropriate permissions, your identifiable collected information and biospecimens may be shared, and,
- Without your additional consent, your identifiable private information and identifiable biospecimens may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies.

Genomic Data Sharing
As part of this study, we will collect and store information about your genes. The DNA contained in your genes holds the instructions that your body uses to grow and function. Your genes are responsible for your physical features such as eye color, blood type, and how your body breaks down medications. Genes can also be responsible for some medical conditions.

Genomic information relates to the structure and function of all of the genetic material in the body.

We will submit your genomic information to a repository managed by the sponsor to be used for scientific purposes. A repository contains information from many people.

We will label your genomic information with a code, instead of your name or other information that people could use to directly identify you. Even so, there is a possibility that when your genomic information is combined with other information available to researchers, either now or in the future, they may be able to identify a group you belong to (like an ethnic group or a disease population) or, less likely, you personally.

You can change your mind later and ask the University of Michigan to have the sponsor remove it. Keep in mind, however, that we cannot take back information that other researchers have already obtained from the repository.

Optional consent to use specimens and/or information for unspecified future research
The study involves the collection of biologic samples including blood, urine and tissue; we anticipate that there may be leftover biological samples after the study-related testing is concluded. The sponsor would also like your permission to keep the leftover biological samples and related information collected in the main study to use in future research. The future research may be similar to this study or may be completely different. Possible future research may try to answer scientific questions about SRK-181 or try to discover new ways to detect or treat cancer.

You can take part in the main study even if you decide not to let the sponsor keep your leftover biological samples and medical information for future research.

If you give the sponsor your permission, the sponsor will use your leftover biological samples and medical information for future research. Even if you give the sponsor permission now, you can change your mind later and ask that your samples be destroyed. (You will need to contact that Principal Investigator in writing to request that your biological materials and data be withdrawn). Keep in mind, however, that once the sponsor has analyzed or shared your leftover biological samples or used your data, the sponsor will not be able to take the information or samples out of the research.

The sponsor may share your leftover biological samples and medical information with other collaborators and researchers, so that they can use it in their research. Your biological samples will never be sold.

Any remaining samples kept and used by or on behalf of Sponsor will include limited information, but will not directly identify you, and will be held by or on behalf of Sponsor for up to 15 years.

As future research will be performed on leftover samples that were already collected during the main study, there are no physical risks associated with donating your samples for use in future research. There are non-physical risks associated with taking part in this optional unspecified future research, such as the risks of genetic testing and the risks associated with the loss of privacy or confidentiality. See Sections 5.1 and 9.1 of this consent form for more information. Future use of your identifiable data and/or specimens will be conducted in compliance with applicable regulatory requirements.

You will not find out the results of future research. Allowing the sponsor to do future research on your leftover blood and tissue samples and medical information will not benefit you directly.

Research with your leftover samples may lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of your information or biological samples. You will not have rights to these discoveries or any proceeds from them.

You will make your choice about whether to have your leftover biological specimens used for unspecified future research at the end of this consent document.

5. INFORMATION ABOUT RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?

Your study doctor and study staff will monitor you closely for side effects. Even with frequent blood tests and other examinations, taking the study intervention involves risks, and some side effects cannot be predicted. Side effects can range from mild to severe and life-threatening. Many side effects will get better when you stop taking the study intervention, but some may be long lasting or may never go away. Side effects may even cause death. You should tell your study doctor immediately about any side effects that you have or any change in how you feel while on this study. If you have side effects, your dose may have to be reduced, or you may have to stop taking the drugs and wait until you feel better before you start again. Your study team may give you medicines or lower your dose of drugs to help lessen side effects. If any side effect is intolerable, you may have to permanently stop taking the drugs.

The known or expected risks are:

This is the first study of SRK-181 in humans and therefore the discomforts and risks are not well known. You will be closely monitored by your study doctor for any side effects or reactions during the study. Your study doctor will discuss with you the possible risks involved with the use of SRK-181.

The following side effects of SRK-181 are based on review of safety data from 54 subjects in this study (19 subjects received SRK-181 alone and 35 subjects received SRK-181 in combination with anti-PD-(L)1). Please review with your study doctor if you don't understand something on the list. Your study doctor will let you know if he or she learns anything new about the safety of the medicine or any new findings that may influence your decision to stay in the study.

This is not a complete list of side effects as there may be side effects that are not known or expected at this time. It is important that you notify your study doctor if you have complaints, or if unusual symptoms occur while you are participating in this study.

As of 21-Nov-2022, the following side effects assessed as "related to SRK-181" by the treating Principal Investigators have been observed in Part A1 subjects who received SRK-181 alone:

- Fatique
- Decreased appetite
- Nausea
- Fatigue (weakness or tiredness)
- Rash (including maculo-papular, blister, pemphigoid and dermatitis bullous)
- Pruritus
- Hypersensitivity (allergic reactions) including rash and eczema

During the study, you may have discomforts and risks from SRK-181 and from the study procedures. Discomforts and risks may vary from person to person. Everyone taking part in the study will be watched carefully for side effects; however, doctors do not know all the discomforts and risks that may happen. There is always the possibility that unknown risks or side effects may occur. These may be mild or very serious, and in some cases may be very serious, long-lasting, or may never go away. There is also a risk of death.

SRK-181 has not been administered to humans before this study and the clinical benefits and risks have not been determined as this is the first time this drug is being tested in humans. There are known side effects of anti-PD-(L)1 antibody therapy, including side effects related to overactive immune cells affecting normal cells and organs in the body. Such side effects can be serious and life-threatening and may lead to death, permanent disability, or organ damage. SRK-181 in combination with anti-PD-(L)1 antibody therapy may increase your risk of having such a side effect or could make them worse than being treated with anti-PD-(L)1 antibody therapy alone.

The effect of SRK-181 on anti-PD-(L)1 antibody therapy is not known. SRK-181 may or may not improve antibody therapy.

Anti-PD-(L)1 antibody therapy has been studied in many (thousands of) patients. Results with other immune stimulating drugs such as anti-PD-(L)1 antibody therapy may have the following potential side effects or discomforts, the most common side effects of immune stimulating drugs may include, but are not limited to the following side effects:

- Infusion or allergic reactions that can sometimes be severe and life-threatening. Symptoms of such a reaction may include rash, itching, flushing, shortness of breath, wheezing, dizziness, fever, chills, shaking, or feeling like passing out

- Reaction at the IV site can include redness, swelling, pain, itching or irritation at the IV site or surrounding tissues
- Fever
- Chills or shaking
- Headache
- Pain in muscles, bones, and joints
- Cough
- Shortness of breath
- Difficulty breathing
- Tiredness
- Difficulty falling or staying asleep
- Dizziness
- Feeling like passing out
- Nausea and/or vomiting
- Decreased appetite
- Weight loss
- Diarrhea or constipation
- Flushing
- Vitiligo (a condition where the color is lost from the skin, causing white patches)
- Itching, itchy skin, or rash

This class of drug has the risk of activating your immune system to attack any organ system in your body and could result in permanent and/or life-threatening side effects.

Pembrolizumab Risks (Updated 03/21/2022)

This risk information for pembrolizumab is current as of the date noted above. Additional safety information may be available for this drug, so it is important that you discuss these risks with your study doctor. There are standard drug information materials specific for pembrolizumab that are available for your review.
Pembrolizumab works by helping your immune system to fight your cancer.
However, pembrolizumab can also cause your immune system to attack normal organs and tissues in your body and can affect the way they work, which can result in side effects. These side effects may be serious (i.e., causing hospitalization or be life-threatening), may result in death, and/or may occur after you stop taking pembrolizumab. These side effects can affect more than one of your normal organs and tissues at the same time.

Most Common, (occurring in 20% or more of subjects):

- Itching of the skin
- Rash
- Fatigue weakness or tiredness)
- Loose or watery stools
- Nausea
- Pain in your belly
- Decreased appetite
- Constipation
- Cough
- Fever

- Pain in muscles
- Shortness of breath
- Not enough thyroid hormone so you may feel tired, gain weight, feel cold, have infrequent or hard stools

Common, (occurring in 5% to 20% of subjects):

- Joint pain
- Back pain
- Pain in your belly
- Loss of skin color
- Not enough thyroid hormone so you may feel tired, gain weight, feel cold, have infrequent or hard stools
- Low levels of salt in the blood that may cause you to feel tired, confused, have a headache, muscle cramps and/or feel sick to your stomach

Less Common, (occurring in 1% to 5% of subjects):

- Inflammation of the lungs so you may feel short of breath and cough. Sometimes this might lead to death
- Too much thyroid hormone so you may feel anxious, angry, have trouble sleeping, feel weak, tremble, sweat, feel tired, have loose and watery stools
- Infusion reaction, where you may feel dizzy or faint, flushed, get a rash, have a fever, feel short of breath, experience a decrease in your blood pressure infusion at the time of receiving your infusion (IV) or just after, or pain at the site of infusion
- Inflammation of the bowels/gut, which may cause severe pain in your belly with loose or watery stools, and black, tarry, sticky stools or stools with blood or mucus
- Inflammation of the skin so you may have peeling of the skin, itchiness, and/or skin redness. The skin inflammation (i.e. peeling, itching and redness) could also be widespread throughout your body. More severe skin reactions may involve the inside of your mouth, the surface of your eye and genital areas, and/or may cause the top layer of your skin to peel from all over your body, which can cause severe infection. These severe conditions can sometimes lead to death.

Rare, (Occurring in less than 1% of subjects):

- Inflammation of the nerves that may cause pain, weakness or tingling in your hands and feet, and may spread to your legs, arms and upper body leading to severe muscle weakness and possible temporary paralysis
- Inflammation of the muscles so you may feel weak or have pain in your muscles
- Inflammation of the pancreas (a gland in your abdomen that controls sugar levels) so you may have severe pain in the top part of your belly that may move to your back, feel sick to your stomach, and vomiting that gets worse when you eat
- Inflammation of the eye so you may have eye redness, blurred vision, sensitivity to light, eye pain, see floaters or have headaches
- Inflammation of the liver that may make you feel sick to your stomach and vomit, feel like not eating, feel tired, have a mild fever, have a pain in the right side of your belly, yellow eyes and skin, and dark urine
- Inflammation of the pituitary gland (a gland in the head), which may cause you to feel sick to your stomach or have headaches, changes in your behavior, double vision, few to no menstrual cycles, weakness, vomiting and dizziness or fainting
- Adrenal glands (glands on top of the kidneys) that may not make enough hormone, which could cause tiredness, weight loss, muscle weakness, feeling faint, joint, muscle and belly aches, nausea, vomiting, loose or watery stools, fever, salt craving, and sometimes darkening of the skin like a suntan

- Type 1 Diabetes, a condition that can cause too much sugar in your blood, feeling thirstier than usual, frequent urination and weight loss. You are likely to need regular insulin shots.
- Inflammation of the kidney so you may pass less urine or have cloudy or bloody urine, swelling and low back pain
- Inflammation of the middle layer of your heart wall that may cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain, shortness of breath and swelling of the legs. You may experience a fast or irregular heartbeat that may cause dizziness or fainting. Sometimes this condition can lead to death
- Inflammation of the thyroid gland, an organ that makes and stores thyroid hormones. This condition may lead to change in your heart rate, blood pressure, body temperature, and the rate at which food is converted into energy.
- A condition that may make you feel weak and tired and might have drooping of the eyelids, blurred or double vision, difficulty swallowing, slurred speech, weakness in your arms and legs, or difficulty breathing
- The formation of small clusters of immune cells (called granulomas) in parts of your body such as your lymph nodes, eyes, skin, or lungs. Depending on where the granulomas forms, you can experience shortness of breath, chest pain, cough, fever or chills.
- Inflammation of the brain with confusion and fever. This may also include: disorientation, memory problems, seizures (fits), changes in personality and behavior, difficulty speaking, weakness or loss of movement in some parts of your body, and loss of consciousness

For disease specific risks please ask your study doctor or refer to the label information.

Pembrolizumab can also cause your immune system to attack normal organs and tissues in your body and can affect the way they work, which can result in side effects that may become serious or life-threatening, and in some cases, may lead to death.

If you have had a solid organ transplant (for example, if you have received a kidney or heart transplant), you may experience rejection of the transplanted organ. Your doctor will monitor you and should tell you what signs and symptoms you should report depending on the type of organ transplant that you have had.

In addition to the above, if you have had an allogeneic stem cell transplant (a procedure in which a person receives blood-forming stem cells from a donor), you may experience graft versus host disease (GvHD), which may include diarrhea, skin rashes, and liver damage, after receiving pembrolizumab. Sometimes this condition can lead to death.

Could I have an allergic reaction?
Sometimes people have allergic reactions to drugs. If you have a very bad allergic reaction, you could die. Some things that may happen during an allergic reaction are:

- Rash
- Itching
- Flushing
- Having a hard time breathing or talking, chest tightness, or wheezing
- A sudden drop in blood pressure (making you feel dizzy or lightheaded or even faint)
- Swelling around the mouth, tongue, throat, or eyes
- A fast pulse
- Sweating
- Abdominal (belly) pain, vomiting, or diarrhea

You should get medical help and contact the study doctor or study staff if you have any of these or any other side effects during the study.

In addition, there is a risk of developing ADA to the study intervention. These could limit the way the study intervention works or even cause allergic reactions that in some cases may be life-threatening. You will be monitored for ADA during the study.

If any discomforts or risks occur, you must tell your study doctor right away.

Your study doctor may give you medications to help lessen or prevent some of the possible discomforts and risks. If a severe reaction to SRK-181 occurs, your study doctor may stop the study intervention.

Pre-clinical studies were conducted with SRK-181, these studies did not reveal any potential side effects.

Could there be any other health problems resulting from doing this research study?
It is possible that receiving SRK-181 in combination with Pembrolizumab, your regular medications or supplements may change how the study intervention, your regular medications, or your regular supplements work together. It is very important that you tell the study doctor or study staff about all medications or supplements you are taking during the study.

Since you will be assigned to use Pembrolizumab, your study doctor can review with you the FDA-approved written information about side effects that can be serious and life-threatening and may lead to death, organ damage, or permanent disability.

You might have side effects or symptoms related to the study intervention while taking part in the study or be injured by a procedure required by the study. Everyone taking part in the study will be watched for any side effects, however the study team does not know all the effects that the study intervention may have on you. There may be side effects which are not known at this time. Ask the study doctor if you have questions about the signs or symptoms of any side effects you read about in this consent form.

Please tell the study doctor or study staff right away if you have any side effects. Please tell them if you have any other problems with your health or the way you feel during the study, whether or not you think these problems are related to the study drug.

Risks from Study Procedures

Electrocardiogram (ECG)

An ECG shows the electrical activity of the heart by placing several small adhesive pads that are attached to wires on your chest and limbs (called leads) and connecting them to a machine that reads the signal. There may be minor discomfort, similar to removing a bandage, when the electrodes taped to your chest are removed.

Echocardiogram (ECHO)

An ECHO is a test that uses sound waves to create a moving picture of the heart, also called a cardiac ultrasound. This test is done to assess how well your heart functions. You may feel some discomfort due to the specific position you may hold during the exam.

IV infusion

The study doctor will give you SRK-181 in combination with Pembrolizumab by infusing it through an IV catheter. IV lines are usually safe and well tolerated and complications are rare, but can include the following problems:

- Irritation of the vein; your skin near the vein could become warm, swell, hurt, or get red
- Damage, infection or inflammation of your vein
- Damage to the skin or tissue around the injection site
- Increase or decrease in electrolyte levels (the number of certain salts and other chemicals in your blood), causing health problems
- A blood clot or an air bubble could form, which could block a blood vessel in another part of your body

Some of these problems could be very serious.

Blood Draws

Collection of blood samples may cause pain, bleeding, bruising, or infection. It is also possible that you may feel lightheaded or faint. Please tell your study doctor or the study nurse if you do not feel well after having your blood drawn at any time during your study participation.

Tumor Biopsy

A piece of a tumor will be removed for testing, at screening and between Day 28 – Day 48. . Potential risks and discomforts that you may experience as a result of the procedure depend upon the location of the tumor. The more common risks/discomforts include pain, bleeding, infection, damage to tissues, and healing complications. Your doctor will further explain any specific risks that may apply based on the procedure, and you will sign a separate consent for the procedure which will provide risk information in more detail. In order to make the procedure more comfortable, you will get a local anesthetic to numb the area. A mild sedative may also be given to you.

MRI (Magnetic Resonance Imaging) Risks

MRIs done for research that use IV contrast have risks similar to MRIs done for clinical care. An MRI scan uses a magnetic field and radio waves to create images of the organs and tissues within your body. Contrast is used to improve the pictures of the inside of the body made by the MRI. Common risks of MRI include: feeling fearful of being in a small enclosed space (claustrophobia) when you are lying inside the MRI scanner, feeling uncomfortable because of the loud noises made by the machines, and feeling uncomfortable with the physical sensations you may feel during the process. You are also exposed to some risk because of the injected contrast, gadolinium-DTPA, which may cause headache, nausea, and local burning sensation.

The contrast agent, gadolinium, has been linked to development of Nephrogenic Fibrosing Dermopathy (NFD), also known as Nephrogenic Systemic Fibrosis (NSF). NFD is a thickening of the skin, organs, and other tissues and

is a rare complication in subjects with kidney disease who undergo an MRI with contrast material. To help prevent this, we will check how well your kidneys work before you have any MRIs. Because of the use of contrast, all female subjects who are able to have children will be required to use adequate birth control. If you have implanted metal objects such as a pacemaker, artificial limbs, or metal joints, you will not be able to have an MRI done, and may not be able to take part in this research.

CT (Computed Tomography) Risks

CT imaging uses ionizing radiation, which increases your risk of cancer. Everyone is exposed to naturally occurring ionizing radiation every day. The amount of radiation exposure from 1 CT scan is approximately comparable to 1-3 years of natural background radiation.

The contrast substance injected during the CT scan may cause pain, burning feeling, sweating, and rarely an allergic reaction that can be serious. If you know you're allergic to iodine, you must inform your doctor immediately. The contrast agent used in the CT scan may cause kidney damage, especially if you're diabetic, dehydrated, and if you're older. In addition, your thyroid function may be affected.

PET-CT Scans

A PET-CT (positron emission tomography-computed tomography) scan is a nuclear medicine imaging test performed with a CT scan. The combined images show the location of abnormal metabolic activity within the body. A small amount of radioactive material (radiopharmaceutical or radiotracer) is injected intravenously before imaging for the PET component of the test. Radioactivity from the radiotracer or radiopharmaceutical is detected by a special camera or imaging device. The CT uses ionizing radiation to obtain pictures of the body. Everyone is exposed to naturally occurring ionizing radiation every day. The amount of radiation exposure from 1 CT scan is approximately comparable to 1-3 years of natural background radiation. The amount of radiation exposure from the radioactive tracer [18F-2-fluoro-2-deoxy-D-glucose (FDG)] is approximately comparable to 2 years of natural background radiation.

Pregnancy Risks

The effects of the study drug on a fetus, a breastfed child, on sperm or the female egg are unknown. Therefore, you cannot participate in this study, if you are pregnant, planning to become pregnant, are breastfeeding a child, or planning to father a baby.

Women

We do not know if SRK-181 in combination with anti-PD-(L)1 antibody therapy, such as Pembrolizumab, will affect mother's milk or an unborn child. Therefore, breast-feeding and pregnant women are not allowed to take part in the study.

If there is ANY chance that you can get pregnant, you must either agree to not have vaginal intercourse or you must use TWO types of birth control (one from each list below) AT THE SAME TIME. These birth control methods must be used from the time of enrollment, all during study intervention including during temporary breaks from therapy, and for at least 90 days (about 3 months) after you stop taking SRK-181 in combination with anti-PD-(L)1 antibody therapy. Subjects who receive pembrolizumab must use appropriate contraception throughout the study and for 4 months after the last dose. The following methods are considered acceptable birth control methods:

Primary forms *Secondary forms*

- tubal sterilization (tubes tied)
- partner's vasectomy
- intrauterine device
- hormonal contraceptives (includes transdermal patch, injectables, implantables)
- male latex condom with or without spermicide
- diaphragm with spermicide
- cervical cap with spermicide
- vaginal sponge (contains spermicide)

Any birth control method can fail. The reports of birth control failing are more frequent for females who use only a single form of birth control. Using two forms of birth control at the same time greatly reduces the chances of pregnancy.
You must have a negative pregnancy test prior to enrolling in the study. If you become pregnant while on this study, the study intervention will be stopped immediately, and the pregnancy will be followed until conclusion. You will be asked for the results of any tests and procedures carried out during your pregnancy and up to the birth. You may also be asked for the results from any evaluation of the baby after the birth.

Men
We do not know if using SRK-181 will affect sperm or an unborn baby. Men must agree to either abstain from sexual activities that could result in pregnancy or use an acceptable form of birth control while taking part in the study and for 90 days (about 3 months) after your last dose of the study intervention. Even if you are surgically sterilized (i.e., have had a vasectomy), if you are sexually active with a woman who is pregnant or could get pregnant, you must agree to use an appropriate method of barrier contraception (latex condom with a spermicidal agent) each time you have sex from the time of signing the informed consent form, and throughout the entire study, and for 90 days (about 3 months) after last dose of study intervention or, you should completely avoid having heterosexual intercourse.

If your partner does become pregnant while you are taking part in the study, you must tell your study doctor immediately who will be able to advise you. In this situation, your partner should be under medical supervision during her pregnancy, and the baby should be under supervision after they are born. Your partner will be asked to give her consent to the collection of information related to both herself as well as the baby.

These risks will be minimized by:
We will minimize the risks by monitoring you carefully. We will provide the usual supportive care that would be routinely given to someone with your condition. If you have side effects from the study intervention, we will make appropriate adjustments as defined by the study protocol. You may need to discontinue the study intervention if the side effects are too serious. If you have signs of infection, you will receive appropriate antibiotics. If you have signs of bleeding, you may need to receive transfusions of platelets, plasma, or red blood cells. If you are at risk of having blood clots, you may receive an anticoagulant (blood thinner). If your hemoglobin level is too low, you may receive a red blood cell transfusion. If you start feeling sick to your stomach, you may be given medications to help reduce nausea. If you have vomiting, you may be given fluids through an IV.

Privacy and confidentiality risks
Additionally, there may be a risk of loss to confidentiality or privacy. For example, if your identity as a participant in this research or your identifiable genetic or health information were disclosed to unauthorized persons, there is the possible risk of discrimination by employers or insurance providers. The researchers believe that the risks of such improper disclosure are very small because strict privacy and confidentiality procedures for this research have been adopted. See Section 9 of this document for more information on how the study team will protect your confidentiality and privacy.

Risks of missing out on another treatment option that could have offered you benefit in treating your cancer. There may be standard of care treatment options available to you for the treatment of your cancer. You may be eligible for such a therapy outside of this study that is known to offer a benefit, including living longer. You and your study doctor should discuss this and confirm there are no other treatment options available to you (this may be because other options have failed, you don't tolerate them or for various reasons, you are not a good candidate for these).

Your decision to participate in this research study will mean you can't participate in other research studies or receive other treatments for your cancer, which otherwise could have been beneficial to you. Before enrolling in this study, it is therefore important to confirm with your study doctor that you are not eligible for other therapies that might be effective in treating your cancer. You should not participate if standard of care therapies could be an option for you.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?
The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors or any other provider or hospital you visit**.**

If you think you have an injury or illness that is related to your participation in this clinical trial, it is important that you tell your study doctor immediately. If you have a clinical trial related injury or accident, the study staff will make sure that you get medical treatment.

You must inform your study doctor immediately if there are any changes in your health/condition, or if you have any concerns regarding the study. If for any reason you are seen by another healthcare provider or admitted to another hospital, you should make known your participation in this research study. These healthcare providers may wish to contact your study doctor to discuss your condition. Your study doctor may need to contact your other doctors if you develop any potentially significant, unexpected diseases or conditions that may have been caused by the study intervention or procedures or are discovered during the study.

5.3 If I take part in this study, can I also participate in other studies?
Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?
You may not receive any direct personal benefits from being in this study. Your disease might stay the same, get better or may even get worse while you are in this study. While doctors hope SRK-181 in combination with Pembrolizumab will be more effective against your cancer compared to available, approved treatment, this is unknown. Information from this study will help doctors learn more about SRK-181 as a potential treatment for your type of cancer. You may or may not benefit as a result of your participation in this study. Results from this study may benefit others in the future.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?

Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. ALTERNATIVES TO PARTICIPATING IN THE STUDY

6.1 If I decide not to take part in this study, what other options do I have?

There may be other ways of treating your condition. Examples of standard of care treatment options available for non-small cell lung cancer (NSCLC), urothelial carcinoma (UC), cutaneous melanoma (MEL), clear cell renal cell carcinoma (ccRCC) and head and neck squamous cell carcinoma (HNSCC) include, but are not limited to:

- NSCLC:
  - Anti-PD-(L)1antibody therapy
  - Platinum-based chemotherapy (alone or in combination with anti-PD-(L)1 antibody therapy)
  - Targeted therapy for EGFR mutation
  - Targeted therapy for ALK aberration
  - Targeted therapy for BRAF mutation
  - Targeted therapy for ROS1 mutation
  - Targeted therapy for KRAS mutation
  - Targeted therapy for NTRK aberration
- UC:
  - Chemotherapy
  - Anti-PD-(L)1 antibody therapy
  - ADC
  - Kinase Inhibitors
- MEL:
  - Anti-PD-(L)1 antibody therapy
  - Anti-PD-(L)1 in combination of different immune checkpoint inhibitors (such as ipilimumab with nivolumab)
  - IL-2 therapy
  - Virus therapy
  - Interferon
  - Targeted therapy for BRAF mutation, or combination of such targeted therapies (such as dabrafenib with trametinib, vemurafenib with cobimetinib, or encorafenib with binimetinib)
  - Targeted therapy for KIT aberration
  - Targeted therapy for NTRK fusion
  - Chemotherapy
  - Targeted therapy for NRAS fusion
  - Anti-LAG3 antibody therapy
- ccRCC:
  - Anti-PD-(L)1 antibody therapy
  - Anti-PD-(L)1 in combination of different immune checkpoint inhibitors (such as ipilimumab with nivolumab)
  - Tyrosine Kinases Inhibitors
  - mTOR Kinase Inhibitors

- IL-2 therapy

- HNSCC:
  - Platinum-based chemotherapy
  - Targeted therapy for EGFR mutation
  - Anti-PD-(L)1 antibody therapy
  - Anti-PD-(L)1 in combination with chemotherapy or targeted therapy
  - Targeted therapy for AR+ tumors
  - Targeted therapy for NTRK aberration
  - Target therapy for HER2+ tumors
  - Kinase Inhibitors

This list of examples is not complete. Please talk to your study doctor about what standard of care treatment options may be available to you for your cancer.

Your other choices may include:

- Taking part in another study.
- Getting treatment only to control the symptoms that you have, also known as palliative care. This type of care does not treat your cancer directly but tries to help reduce pain, tiredness, loss of appetite and other problems caused by the cancer.
- Getting no treatment.

Your doctor can tell you more about these other treatments, their risks and their possible benefits. You should have this discussion about the risks and benefits or other alternatives prior to making your decision about whether or not you wish to take part in this research study.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?

You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 “Contact Information”.

You are free to partially or completely end your participation in the study. An example of partially ending your participation would be to discontinue receiving study intervention, while still allowing continuation of study follow-up procedures.

Please note that any information collected before you withdraw will be kept and used as outlined in this consent form.

Please note that even if you withdraw consent for further follow-up or contacts, if the study doctor becomes aware of additional safety information this will be reported to the sponsor in order to comply with legal or regulatory requirements.

You may participate in an optional sub-study to allow the storage of your research samples for future use (see “Optional consent to use specimens and/or information for unspecified future research” in Section 4.4, above). Please note that if you decide to withdraw from the main study and had agreed to participate in the optional sub-

study, you will not be automatically withdrawn from the optional sub-study. If you wish to also withdraw your samples from the optional sub-study, you will need to tell your study doctor.

7.2 Could there be any harm to me if I decide to leave the study before it is finished?
Tell the study doctor if you are thinking about stopping or decide to stop. It is important to tell the study doctor if you are thinking about stopping so any risks can be evaluated by your doctor. The study doctor will also tell you how to stop safely and discuss what follow-up care and testing could be most helpful for you. If you decide to leave the study before it is finished, please tell your study doctor or one of the researchers listed in Section 10 "Contact Information" (below).

7.3 Could the researchers take me out of the study even if I want to continue to participate?
Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- The researchers or your study doctor believe that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?
The study will pay for research-related items or services that are provided only because you are in the study. If you are not sure what these are, see Section 4.1 above or ask the researchers for a list. If you get a bill you think is wrong, call the researchers' telephone number listed in Section 10.1.

You will not be charged for SRK-181 and pembrolizumab.

You or your health plan will pay for all the things you would have paid for even if you were not in the study, like:

- Health care given during the study as part of your regular care
- Items or services needed to give you study drugs or devices
- Monitoring for side effects or other problems
- Deductibles or co-pays for these items or services.

If you do not have a health plan, or if you think your health plan may not cover these costs during the study, please talk to the researchers listed in Section 10 below or call your health plan's medical reviewer.

The study team has given you instructions about this research study. It is important that you follow these instructions carefully. If you get sick, have a medical complication, or are injured as a result of your being in the study, call Dr. Vaishampayan immediately, at 734-936-7813 or 734-936-4000 (Hospital Operator – 24-hour paging). The doctor will either treat you or send you to another doctor for treatment. You will get free medical care for any complication, injury, or illness caused by the study intervention, device, or procedure. The study sponsor and the study doctor are responsible for determining whether your condition was the result of your participation in the study. The study sponsor will pay for your treatment only if the need for treatment has been caused by the study intervention, device or procedure. This means that you or your health plan must pay for any treatment that is part of your usual medical care or that is related to a medical condition you had before participating in the study.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

8.2 Will I be paid or given anything for taking part in this study?
You will receive a payment of $38.76 per visit (screening visit, study intervention visits, and End of Study Intervention visit) to help cover the cost of travel and expenses.

You will be reimbursed for up to 14 hotel stays during your study participation for up to $150 if you travel more than 150 miles one way. You may also be reimbursed for travel expenses during the study. You will be required to provide receipts to receive reimbursement for hotel stays and travel expenses. Mileage to the study site will be calculated via Google maps and reimbursed at the current IRS rate. Reimbursement for long-distance travel will require sponsor pre-approval. You will receive payment after each visit or at least monthly for the visits you complete.

If you withdraw from the study, you will still receive the reimbursement for expenses incurred that are associated with the study appointments you present for and for which you have receipts. Generally, it is about 2 weeks from the time you submit receipts until you receive your reimbursement.

8.3 Who could profit or financially benefit from the study results?
The company whose product is being studied: Scholar Rock, Inc.

The University of Michigan is receiving payments from Scholar Rock, Inc. to support the activities that are required to conduct the study.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the data or discoveries. You will not have rights to these discoveries or any proceeds from them.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how your privacy and the confidentiality of your research records will be protected in this study, and any sub-studies described in this document.

9.1 How will the researchers protect my privacy?
Your participation will occur at Michigan Medicine. Your data will be kept confidential, to the extent permitted by applicable laws, in the following manner:

- Your name will not be used in any reports about the study
- You will be identified only by a study code: a subject ID number, and initials
- Your identifying information will be kept secure

Despite these protections, some study data may contain information that could be used (perhaps in combination with other information) to identify you (e.g., initials, date of birth).

Your study data that is collected for this research will be kept for a minimum of 15 years.

Genetic Information Nondiscrimination Act (GINA)
The federal Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Under this law:

- Health insurance companies and group health plans may not request your genetic information that we obtain from this research
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums
- Employers with 15 or more employees may not use your genetic information that we obtain from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment

GINA does not apply to the following groups; however, these groups have policies in place that provide similar protections against discrimination:

- Members of the US Military receiving care through Tricare
- Veterans receiving care through the Veteran's Administration (VA)
- The Indian Health Service
- Federal employees receiving care through the Federal Employees Health Benefits Plans

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 Web site at any time.

9.2 What protected health information (PHI) about me could be seen by the researchers or by other people? Why? Who might see it?
Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study.

Medical information and billing records are protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA). This type of information is called protected health information (PHI). PHI about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- Mental health care records (except psychotherapy notes not kept with your medical records)
- Alcohol/substance abuse treatment records
- HIV/AIDS status
- Sexually transmitted disease and/or other communicable disease status
- Genetic counseling/genetic testing records
- Health plan/health insurance records
- All records relating to your condition, the treatment you have received, and your response to the treatment
- Billing information
- Demographic information
- Personal identifiers

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- University, Food and Drug Administration (FDA) and/or other government officials, auditors, and/or the IRB may need the information to make sure that the study is done in a safe and proper manner.
- Study sponsors or funders, or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly
    - Learn more about side effects
    - Analyze the results of the study
- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular Michigan Medicine medical record.
- If you receive any payments for taking part in this study, the University of Michigan accounting department may need your name, address, Social Security number, payment amount, and related information for tax reporting purposes.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be presented and published in an article, but would not include any information that would let others know who you are. The sponsor may share the study data with third parties for research and development of drugs and diagnostics. The study data may be submitted to regulatory authorities for purpose of applying for approval of the study drug or other drug candidates and diagnostics. It may also be used to better understand various cancers.

You have the right to access and correct the information collected about you during this study as long as the study doctor keeps your medical information. You may also ask for and get a copy of your personal data and test results at no charge and have it sent to your regular doctor or specialist. You will only be able to receive copies of the notes and tests that your study doctor and study staff keep in their records including any information that is part of your usual medical care but you will not be able to receive copies of study information such as exploratory lab tests.

9.3 What happens to information about me after the study is over or if I cancel my permission to use my PHI?
As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan "Notice of Privacy Practices". This information is also available on the web at http://www.uofmhealth.org/patient+and+visitor+guide/hipaa. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.4 When does my permission to use my PHI expire?
Your permission does not expire, unless you cancel it. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below). If you withdraw your permission, you may no longer be eligible to participate in this study.

10. CONTACT INFORMATION

10.1 Who can I contact about this study?
Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator:	Ulka Vaishampayan, MBBS
Mailing Address:	University of Michigan 1500 East Medical Center Drive Rogel Cancer Center 7217, SPC 5948 Ann Arbor, MI 48109
Telephone:	734-936-7813 (Office) 734-936-4000 (Hospital Operator – 24-hour paging)

You may also express a question or concern about a study by contacting the Institutional Review Board listed below.

University of Michigan Medical School Institutional Review Board (IRBMED)
2800 Plymouth Road
Building 520, Room 3214
Ann Arbor, MI 48109-2800
Telephone: 734-763-4768 (For International Studies, include the appropriate calling codes.)
Fax: 734-763-1234
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.
When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

You will receive a copy of the signed and dated informed consent document.

Your signature in the next section means that you have received copies of all of the following documents:
This "Consent to be Part of a Research Study" document. (*Note: In addition to the signed and dated copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*

12. SIGNATURES

Consent/Assent to Participate in the Research Study

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Consent/Assent for use of leftover biological samples for unspecified future research

This project involves the option to allow the sponsor to keep your leftover identifiable specimens/data for use in future research. I understand that it is my choice whether or not to allow this. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

_____ Yes, I agree to have my samples retained, stored and used as outlined in the consent form.

_____ No, I do not agree to let the sponsor keep my specimens for future research.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Principal Investigator or Designee

I have provided this participant and/or his/her legally authorized representative(s) with information about this study that I believe to be accurate and complete. The participant and/or his/her legally authorized representative(s) indicated that he or she understands the nature of the study, including risks and benefits of participating.

Legal Name: _____

Title: _____

Signature: _____

Date of Signature (mm/dd/yy): _____