The Ohio State University Combined Consent to Participate in Research and HIPAA Research Authorization

Study Title:	**A Phase IB Study to Assess the Safety and Efficacy of Neoadjuvant Administration of Autologous Tumor Infiltrating Lymphocytes (LN-144/Lifileucel) and Pembrolizumab for Treatment of Patients with Locally Advanced (Stage IIIB-D/IV) Melanoma**
Principal Investigator:	**Richard Wu, MD**
Sponsors:	**The Ohio State University and IOVANCE Biotherapeutics**
Drug Provided by:	**IOVANCE Biotherapeutics**

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.
- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

Key Information About This Study

The following is a short summary to help you decide whether or not to be a part of this study. More detailed information is listed later in this form.

You are invited to take part in a clinical research study. Before you decide to take part in this clinical research study, you need to understand the risks and benefits. This consent form provides information about the clinical research study. The Study Doctor or a member of the study team will be available to answer your questions and provide further explanation. If you

agree to take part in the clinical research study, you will be asked to sign this consent form. This process is known as informed consent. You may take home an unsigned copy of this consent form to think about the clinical research study and discuss it with family or friends. After agreeing to participate and signing this consent form, you will be provided a full copy of the signed consent.

The research study is being funded by Iovance Biotherapeutics Inc. Iovance Biotherapeutics Inc. is providing research support and study drug for this research study. Dr. Richard Wu is the principal investigator of this study at The Ohio State University Comprehensive Cancer Center (OSU).

Your general practitioner/usual doctor may be informed about your participation in this clinical research study.

The Investigational Product (i.e., study drug) to be used in this clinical research study is LN-144, which is a cellular product also called "tumor infiltrating lymphocytes" or TIL. The LN-144 Investigational Product is made up of specialized white blood cells called lymphocytes or "T cells" that are derived from your tumor after a small piece is obtained by surgical removal. This piece of your own tumor is sent to a centralized manufacturing facility where T cells that have infiltrated your tumor are isolated and grown to create the Investigational Product LN-144, which are infused back into your body. TIL therapy with LN-144 involves expanding and activating your tumor-involved lymph node(s)-derived T cells in vitro (in tissue culture) and then infusing the cells back into you where they may then attack your tumor. The LN-144 Investigational Product is given with other medications that together make up the therapy with LN-144. The other medication given with LN-144 therapy includes receiving an approved preconditioning regimen of chemotherapy medications (cyclophosphamide combined with mesna, and fludarabine) prior to the infusion of LN-144 that prepares your body to receive the LN-144 in a way that allows the T cells the best opportunity to attack your tumor. After receiving the LN-144 infusion, you will receive a medication called interleukin-2 (IL-2, Proleukin®), which is a naturally occurring protein that helps white blood cells/T cells regulate their immune response.

"Investigational" means that it has not been approved for sale in the United States by the U.S. Food and Drug Administration (FDA) or any other health authority. To date, the Investigational Product LN-144, has been given to over 300 humans, who have participated in clinical research studies sponsored by Iovance Biotherapeutics Inc.

Pembrolizumab (Keytruda®) is FDA approved and commercially available in the United States of America (USA), and in other countries for the treatment of several disease types, including your type of cancer.

Dr. Joal Beane, MD a researcher helping to perform this study, could benefit financially from the sale of the investigational product **LN-144 a cellular product also known as TIL (tumor infiltrating lymphocytes)** being tested. A conflict-of-interest committee at Ohio State has reviewed this information and determined that Dr. Beane's involvement presents no

additional significant risk to the study's participants. Any questions about this information can be answered by **Dr. Richard, Wu, MD, PHD 614-293-4320.**

1. Why is this study being done?

You are invited to take part in this clinical research study because you have been diagnosed with Locally Advanced Stage IIIB-D Melanoma. The purpose of this clinical research study, which will be performed at OSU in collaboration with Iovance Biotherapeutics Inc., is to find out if an Investigational Product, called LN-144 (manufactured by Iovance Biotherapeutics Inc.) can help to control your disease when given together with a medication, named pembrolizumab (Keytruda). The study will also look to see if the combination of the two medications is safe and beneficial in the treatment of patients with locally advanced stage IIIB-D or stage IV (metastatic) melanoma.

2. How many people will take part in this study?

It is expected that 20 patients with locally advanced stage IIIB-D or stage IV (metastatic) melanoma will be enrolled in this clinical research study at OSU with the goal of having 15 eligible participants finish the study.

3. What will happen if I take part in this study?

What procedures are involved?

Tests and procedures that would be performed for your regular cancer care whether you are on this study or not are called "standard of care". All the tests and procedures listed below will be performed at your study visits, should you choose to participate in this study.

If you decide to participate in this clinical research study, after signing the consent form, you will first need to have some tests done to see if you meet the requirements to continue in this clinical research study. These tests are called screening tests and the screening period of this clinical research study, may take up to 28 days.

If you decide to be in this study, you might have to stop taking your regular medication, therapy, or supplement during the study.

During the screening period, you may have multiple visits, in which the following procedures will be performed to determine if you are eligible to continue in this clinical research study:

Screening Period:

<u>As part of research:</u>

- Informed consent discussion if you want to take part in this study, and only if you consent will the following activities/assessment take place

- Heart test to measure electrical activity across the heart (electrocardiogram [ECG])
- Heart function test (echocardiogram [ECHO] or a multigated acquisition [MUGA] scan)
- Heart stress test that shows how well blood flows into your heart will be done if you are 60 years old or older, or if you have a previous history of heart disease.
- Lung function tests using a spirometry
- Blood sample (approx. 5 mL= 1 teaspoon) to test your exposure to specific viruses or bacteria including HIV, Hepatitis, Syphilis, Herpes viruses, Epstein-Barr virus (EBV) and CMV (cytomegalovirus), a common virus.
- Urine sample test
- Assessment of side effects
- Blood sample (approx. 15 mL = 1 tablespoon) to assess your general health, how your blood clots, and how well your thyroid is working
- HLA testing is to learn about the types of proteins found on the surface of your white blood cells

<u>As routine standard of care:</u>

- Demographic information (date of birth, gender, race, and ethnicity)
- Medical and cancer history (prior radiotherapy, cancer-related and significant surgery, and systemic therapy)
- Physical examination including height and weight
- Vital signs (blood pressure, heart rate, respiratory rate, and body temperature)
- Evaluation of your current health status and confirmation of your diagnosis
- Review of current medications you are taking
- Blood sample (approx. 5 mL= 1 teaspoon) to determine the status of your kidneys
- Liver Function Tests
- Blood sample for pregnancy test, if you are a woman of childbearing potential
- CT, MRI, or PET scan of your body (chest, abdomen, pelvis and other areas if you have disease there)
- Brain MRI (depending on your disease involvement)

Tumor Collection:

If you meet the study requirements, you will have surgery to remove part of your tumor. Your Study Doctor will discuss the procedure in more detail with you. You may be admitted to the hospital for the collection of your tumor. There will be an additional consent form for this procedure per the institutional standards of the hospital. The tumor lesion that is removed will be shipped to a central manufacturing facility chosen by Iovance Biotherapeutics Inc. (a company supporting this study) for processing and generation of the Investigational Product, LN-144.

At the visit to remove your tumor, the following procedures will be performed:

As part of research:

- Blood sample (30 mL total for this visit = 2 tablespoons) for biomarkers (looking at your specific blood molecules)
- Surgery and tumor collection
- A small section of the tumor tissue collected will be analyzed for your biomarker status (looking at biological molecules or cells found in blood that may be used to see how well you respond to treatment with LN-144) including PD-L1 status (PD-L1 also known as Programmed Cell Death Ligand 1, is a protein found on immune cells)
- Assessment of side effects

As routine standard of care:

- Review of current medications

Samples collected during the tumor collection visit will be used to manufacture LN-144.

Baseline Visit

You will have a Baseline visit to be scheduled 2 to 3 weeks before your planned LN-144 infusion day. At this visit the Study Doctor will reassess your general health to determine that you still meet the study requirements. The following procedures will be performed:

As part of research:

- Review of Study eligibility
- Heart test to measure electrical activity across the heart (electrocardiogram [ECG])
- Urine sample test
- Assessment of side effects

As routine standard of care:

- Physical examination
- Vital signs (weight, blood pressure, heart rate, respiratory rate, and body temperature)
- Evaluation of your current health status
- Review of current medications
- Blood sample to assess your general health and liver function
- (approx. 15 mL = 1 tablespoon)
- CT, MRI or PET scan of your body (chest, abdomen, pelvis and other areas if you have disease there)
- Brain MRI

You will receive a single dose of pembrolizumab (Keytruda®) by intravenous infusion approximately 2 weeks before receiving LN-144.

Study Drug Administration

Before you begin the preconditioning chemotherapy, your Study Doctor will ensure that the tumor infiltrating lymphocytes (TIL) from your tumor are growing to produce the Investigational Product, LN-144. If your cells are not growing, your Study Doctor will discuss treatment options other than this clinical research study with you.

If LN-144 can successfully be created in the facility, you will be hospitalized and begin to receive preconditioning chemotherapy (cyclophosphamide and fludarabine) to help prepare your body to receive LN-144. The chemotherapy treatment will begin seven (7) days before receiving LN-144.

LN-144/TIL manufacturing will take up to 23 days to manufacture and up to 10 days further for testing to release the product, so your inpatient admission and preconditioning chemotherapy may be delayed by up to an additional 10 days.

The preconditioning chemotherapy regimen given to you by intravenous infusion (into a vein). The chemotherapy, cyclophosphamide, is given with another medication called mesna. Mesna is meant to either reduce or prevent side effects of the cyclophosphamide chemotherapy. You will be in the hospital for two (2) days when you are receiving cyclophosphamide with mesna. You may receive the fludarabine portion of the preconditioning chemotherapy in the hospital (5 days) or on an outpatient basis.

If you were not hospitalized during the previous study days, you will be admitted to the hospital a day or two before you receive the LN-144 infusion, and you will have to stay there until you have completed treatment with interleukin-2 (IL-2) and your Study Doctor feels you can be discharged.

You will receive a single dose of LN-144 by intravenous infusion. After you receive LN-144, you will receive IL-2 by vein. IL-2 helps LN-144 to "attack" the tumor. Your dose of IL-2 may change while you are on study. You may be given standard drugs to help decrease the risk of side effects.

Day	Investigational Product	Hospital Stay Length
Day 7 and 6 prior to LN-144 infusion	Cyclophosphamide with Mesna	2 days
Day 5, 4, 3, 2, and 1 prior to LN-144 infusion	Fludarabine	5 days (or given on outpatient basis)
Day of LN-144 infusion	LN-144	1 day
Day 1, 2 and3 after LN-144 infusion	IL-2	3 days
Total		**Up to 11 Days**

Schedule of Procedures

Procedures	Day 7 prior to LN-144 infusion	Day 6 prior to LN-144 infusion	Day 5, 4, and 3 prior to LN-144 infusion	Day 2 prior to LN-144 infusion	Day 1 prior to LN-144 infusion
As part of research					
Urine sample test	☐	☐	As needed per study doctor		
Antibiotic medications	As needed per study doctor				
Supportive medications as required (such as for prevention of nausea, diarrhea or fever)	☐	☐	☐	☐	☐
Assessment of side effects	☐	☐	☐	☐	☐
As routine standard of care					
Physical examination	☐			☐	☐
Vital signs (weight, blood pressure, heart rate, respiratory rate, and body temperature)	☐	☐	☐	☐	☐
Evaluation of your current health status	☐				
Review of current medications	☐	☐	☐	☐	☐
Blood sample (approx. 15 mL=1 tablespoon) to assess your general healt	☐	☐	As needed per study doctor		
Cyclophosphamide infusion (preconditioning chemotherapy) 60 mg/kg over 2 hours	☐	☐			
Fludarabine 25 mg/m^2 infusion (preconditioning chemotherapy) over 3(minutes			☐	☐	☐
Mesna (chemotherapy supportive care) 15 mg/kg infusion over 2 hours	☐	☐			

Blood sample (approx. 5 mL = 1 teaspoon) for pregnancy test, if you are a woman of childbearing potential	☐				

On the day of your scheduled LN-144 infusion, the following procedures will be performed:

As part of research:

- Urine sample test
- LN-144 infusion
- Antibiotic medications
- Assessment of side effects

As routine standard of care:

- Physical examination
- Vital signs (weight, blood pressure, heart rate, respiratory rate, and body temperature)
- Review of current medications
- Blood sample (approx. 15 mL = 1 tablespoon) to assess your general health and liver function
- Blood sample (approx. 5 mL = 1 teaspoon) for pregnancy test, if you are a woman of childbearing potential

During the four (4) days following your LN-144 treatment day, the following procedures will be performed:

Procedures	**Day 1 after LN-144 infusion**	**Day 2 and Day 3 after LN-144 infusion**	**Day 4 after LN-144 infusion**
As part of research			
Blood sample (approx. 30 mL = 2 tablespoons) for biomarkers (looking at your specific blood molecules)	☐		☐
Urine sample test	☐	☐	☐
IL-2 infusion	☐	☐	☐
Antibiotic medications	As needed per study doctor		
Assessment of side effects	☐	☐	☐
As routine standard of care			

Physical examination	☐		☐
Vital signs (weight, blood pressure, heart rate, respiratory rate, and body temperature)	☐	☐	☐
Review of current medications	☐	☐	☐
Pulse Oximetry, measurement of the oxygen in your blood using a finger clip	☐	☐	☐
Blood sample (approx. 15 mL = 1 tablespoon) to assess your general health and liver function	☐	☐	☐
Filgrastim (medication to increase your neutrophil count, a type of white blood cell) injection under the skin	☐	☐	
Fluconazole (anti-fungal medication) by mouth	As needed per study doctor		
Supportive medications as required (such as for prevention of nausea, diarrhea or fever)	☐	☐	☐

You will be asked to return to clinic for follow-up visits scheduled at Day 28 (Week 4), Day 42 (Week 6), Day 70 (Week 12), Day 126 (Week 18), Month 6 (Week 24), and then every 3 months thereafter until disease progression or commencement of new anticancer therapy.

You will receive maintenance doses of pembrolizumab (Keytruda®) by intravenous infusion on Day 28 (Week 4) and every 6 weeks thereafter for up to a year.

Procedures	**Day 28 W4**	**Day 42 W6**	**Day 84 W12**	**Day 126 W18**	**Month 6 W24 Every 3 Months thereafter until EOA**
As part of research					
Blood sample (approx. 30 mL = 2 tablespoons) for biomarkers (looking at your specific tumor genes)		☐	☐		☐
Urine sample test	☐	☐	☐	☐	☐
Antibiotic medications	As needed per study doctor				
Assessment of side effects	☐	☐	☐	☐	☐
Day 42/W6 post treatment biopsy (tumor sample)		☐			

Assessment of treatment response		☐	☐	☐	☐
As routine standard of care					
Physical examination	☐	☐	☐	☐	☐
Vital signs (weight, blood pressure, heart rate, respiratory rate, and body temperature)	☐	☐	☐	☐	☐
Evaluation of your current health status	☐	☐	☐	☐	☐
Review of current medications	☐	☐	☐	☐	☐
Blood sample (approx. 15 mL = 1 tablespoon) to assess your general health and liver function	☐	☐	☐	☐	☐
Blood sample (approx. 5 mL = 1 teaspoon) to determine how well your thyroid is working	☐				
Blood sample (approx. 5 mL = 1 teaspoon) to determine the status of your kidneys			☐		
CT, MRI or PET scan of your body (chest, abdomen, pelvis and other areas if you have disease there)		☐	☐	☐	☐
Brain MRI		☐	☐	☐	☐
Valacyclovir or acyclovir (anti-viral medication) if applicable	As needed per study doctor				
Fluconazole (anti-fungal medication)	As needed per study doctor				
Blood sample (approx. 5 mL = 1 teaspoon) for pregnancy test, if you are a woman of childbearing potential	☐	☐	☐	☐	☐

After your Month 6 visit you will have a visit every 3 months until Month 36, withdrawal of consent, death, or termination of study by OSU (the Sponsor), whatever will occur first.

After you have completed your Treatment and Assessment Period, you will be asked to complete an End of Assessment (EOA) visit. The End of Assessment procedures to be performed are:

<u>As part of research:</u>

- Urine sample test
- Assessment of side effects
- Assessment of treatment response

As routine standard of care:

- Physical examination
- Vital signs (weight, blood pressure, heart rate, respiratory rate, and body temperature)
- Evaluation of your current health status
- Review of current medications
- Blood sample to assess your general health
- (approx. 15 mL = 1 tablespoon)
- Blood sample to determine how well your thyroid is working
- (approx. 5 mL = 1 teaspoon)Blood sample (approx. 5 mL = 1 teaspoon) for pregnancy test, if you are a woman of childbearing potential
- CT, MRI, or PET scan of your body (chest, abdomen, pelvis and other areas if you have disease there)
- Brain MRI

What is expected from you?

When deciding whether to participate, consider if you are able and willing:

- To follow the instructions of the study staff
- To keep your study visit appointments
- To tell the Study Doctor truthfully about your complete medical history
- To provide tumor tissue samples, blood samples, and urine samples
- To be available for telephone conversations with the study staff
- To report any new problems, illnesses, or changes in medication during the study
- To consider other treatment options that are available to you

Following the end of assessment visit, you will enter long-term follow-up (LTFU). You will be contacted by telephone or other means (such as e-mail) approximately every 3 months and for up to 36 months (3 years) to confirm the status of your disease and whether you have started another anticancer therapy. Your Study Doctor (or appointed delegate) may seek to establish your long- term health status for a period of not more than 3 years after receiving LN-144, by accessing your hospital records, or publicly available sources such as national registries and, newspaper obituaries. Attempts may also be made to contact you or your relatives to ascertain this information. If you do not want this information about you to be collected, you may record your objection with your Study Doctor at any time.

Your Blood and Tumor Samples

Some of your blood will be used to test for HIV and other communicable diseases (diseases that can be spread from one person to another) as described earlier. Ask the study doctor or study staff which diseases your blood will be tested for. The study doctor and study staff will tell you if the test results are positive.

If you are a woman who can have children, your blood will be tested to see if you are pregnant. The study doctor or study staff will tell you if the pregnancy test results are positive. The results of the pregnancy test must be negative for you to be in the study.

The sponsor/supporter may use tumor tissue and blood you provided during the study for genetic research.

- We will study your samples to improve our understanding of the way changes in genes can affect the risk of cancer and other diseases. Specifically, the genetic research will look for changes in your genes that may cause tumors to form and grow. The research will also explore how genetic differences may influence the way someone responds to LN-144. While doing this research, the sponsor will compare the genes in your tumor cells before and after your treatment with LN-144.
- Genes are the "blueprints" for our bodies. Sometimes genes may have changes that occur during your lifetime that can affect the way a gene works. These changes may cause cells to grow rapidly and abnormally, and become a cancer that you cannot pass on to your family members (somatic mutation). However, some people develop cancer because they were born with a mutation in a gene. People who develop cancer because of a genetic mutation usually inherit this genetic change from their mother or their father (germline mutation). Other family members (brothers, sisters, and children) may share this same mutation. Most people with cancer did not develop their disease because of an inherited mutation.
- After your samples have been analyzed, if any part of them is left over, the material will be stored for use in research. The samples will be stored for up to 5 years after the study ends and, if they have not been used by the end of that period of time, they will be destroyed.
- Neither you nor your doctor will be given the results of any genetic research testing done on your samples. If you or your family are interested in learning more about inherited risk factors for cancer, ask your study doctor.

A Federal law, the 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 generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get 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 get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, long-term care insurance, or if you are a member of the military. The results of testing your tissue and blood will be used only for research, and not to guide your medical care.

Please check Yes or No. Your medical care will not be affected, no matter what you decide to do.

I agree that my tumor tissue and blood collected during the study may be used for the genetic research described above.

❑ Yes ❑ No

4. How long will I be in the study?

Depending on your participation in the study, your participation in the study can last up to 3 years (36 months).

COULD THE STUDY OR MY PART IN IT STOP BEFORE THE END?

This study or your part in the study may be stopped before it has finished without your consent for several reasons.

The Sponsor may stop the study or put the study on hold for the following reasons:

- The study treatment is shown not to work.
- The study treatment is shown to work, and there is no need for further study.
- A decision is made by the government health authorities or Institutional Review Boards/Independent Ethics Committees to stop the study.
- There is an unexpected, significant, or unacceptable risk to patients.
- Not enough patients agree to take part in the study within a reasonable time period.
- The information gained from the study is not complete or able to be understood.
- The Sponsor or Study Supporter makes a business decision to stop the study.

The Study Doctor may stop your part in the study for the following reasons:

- You have serious side effects.
- You did not keep appointments.
- You did not take the study treatment as directed.
- You began taking other treatments that are not allowed in the study.
- You become pregnant.

5. Can I stop being in the study?

You may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University.

CAN I CHANGE MY MIND ONCE THE STUDY HAS STARTED?

- You may stop taking part in the study at any time, without having to give any reasons. You will still receive care for your condition and will not lose any benefits to which you are otherwise entitled. If you decide to withdraw your consent, please notify the study staff as soon as possible. You may be asked to go to the clinic for a final visit or follow-up. If you do not wish to receive the LN-144 product, your TIL samples may still be used for research and development purposes unless you tell your Study Doctor in writing that you do not wish for it to be used for this purpose.
- If your participation stops, the Study Doctor will still be able to use the information collected about you prior to your withdrawal from this study. Information that has already been sent to the Sponsor cannot be withdrawn. Samples that you provided during the study will continue to be analyzed unless you tell your Study Doctor in writing that you wish for your samples to be destroyed.

6. What risks, side effects or discomforts can I expect from being in the study?

There is a risk of loss of confidentiality of your information that is used in this study.

Side effects from the study treatment

You may experience side effects and/or discomforts while taking part in the study. Everyone taking part in the study will be watched carefully for any side effects, as doctors do not know all the side effects that may happen. Side effects may go away after the treatment is stopped, but they may last a long time or forever. Side effects may be mild or very serious, resulting in life-threatening situations leading to intubation (the process of inserting a tube through the mouth and throat to make it easier to get air in your lungs), dialysis (a treatment that filters and purifies your blood using a machine), or other interventions. Some side effects may also be fatal. You must talk to your Study Doctor about any side effects that you have while taking part in the study. He/she may give you treatment for any side effects that you experience. Every effort will be made to watch you for possible side effects using blood and urine tests and examinations.

Risks Associated with LN-144

The LN-144 investigational product contains tumor infiltrating lymphocytes (TIL), human serum albumin (HSA), human recombinant interleukin-2 (IL-2) and small amounts of antibiotics known as gentamicin and streptomycin, which belong to a group of antibiotics

known as 'aminoglycosides.' The frozen LN-144 product also contains ingredients meant to protect the drug product while frozen, such as dimethyl sulfoxide (DMSO) and dextran-40. Allergic reaction, which is also sometimes known as an infusion related reaction, has been associated with at least one of the above-mentioned formulation components. You may get fever, chills, increased heart rate, rash, low blood pressure that may make you feel dizzy or faint, shortness of breath, swelling of the face or throat, cough, chest tightness or wheezing. Sometimes, a more severe allergic reaction known as anaphylaxis may occur, and it will require immediate treatment with an injection of epinephrine, corticosteroids or inhaled bronchodilators. In rare cases, this more severe allergic reaction may require intubation (the process of inserting a tube through the mouth and throat to make it easier to get air in your lungs).
Patients who have known allergy to any component of the LN-144 infusion product formulation are excluded from the study. To reduce the chances of getting an allergic reaction, you will receive medicines like acetaminophen and diphenhydramine, or other appropriate medication per your Study Doctor. You will be monitored for any signs or symptoms of allergic reaction during your LN-144 infusion.

Other risks associated with DMSO, one of the components of the cryopreserved or frozen LN-144, is the onset of a "warming" sensation as the LN-144 product is infused into the body. This sensation is temporary and resolves on its own. In addition, DMSO can spread out of the lungs and may be present when you breathe out, causing a taste or smell similar to rotten eggs.

In patients who are being treated for melanoma, the following other risks associated with the TIL formulation have been observed:

- Vitiligo, a nonserious skin condition in which patches of the skin turn lighter than the surrounding skin; and

- Inflammation of the middle layer of the eye (uveitis) that may result in symptoms such as redness, pain, light sensitivity, blurred vision, and dark floating spots in the field of vision. Most people who get early treatment for uveitis have little, if any, long-term vision problems. Treatments can stop the disease from worsening and reverse any eye symptoms or changes in vision. Severe forms may need long-term treatment. Severe disease is more likely to cause vision loss.

Please notify your Study Doctor and/or site staff immediately if you begin experiencing any of the above symptoms so that your condition can be checked, and any necessary treatment can be given.

Please discuss with your Study Doctor about the possible risk of these components in the LN-144 study product.

LN-144 is an investigational new drug; therefore, you may experience side effects that are not yet known and potentially serious or life-threatening. Please notify your Study Doctor and/or

site staff of any side effects that you are experiencing. Once LN-144 is stopped, it is not known how long a side effect may last.

To date one patient on the study after receive treatment patient experienced hemolyisis (hemolytic anemia a condition where your red blood cells breakdown faster than your body can replace them). The patient has since recovered and continued to participate in the study. The hemolytic anemia was possibly related to Pembrolizumab or to LN-144 or to the Non-Investigational Treatment Prophylactic Antibiotic Dapsone. You will be closely monitored for side effects from the treatment. If your treating physician or study doctor determines you need to take the prophylactic antibiotic Dapsone, a blood test for G6PD (an enzyme in your blood that affects your red blood cells) to be certain you are not deficient in this enzyme and that it is safe for you to be treated with Dapsone. If you are found to have G6PD deficiency your doctor will discuss this with you.

Side effects of other study treatments

Risks Associated with Pembrolizumab

COMMON, SOME MAY BE SERIOUS In 100 people receiving pembrolizumab, more than 20 and up to 100 may have:		
• Itching of skin	• Loose or watery stools	• Cough

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving pembrolizumab, from 5 to 20 may have:		
• Joint pain • Back pain • Rash • Fever • Stomach pain	• Low level of salt in the blood that may cause you to feel tired, confused, headache, muscle cramps or upset stomach	• Loss of skin color • Not enough thyroid hormone so you may feel tired, gain weight, feel cold, have infrequent or hard stools

RARE, AND SERIOUS In 100 people receiving pembrolizumab, 5 or fewer may have:		
• Inflammation of the lungs so you may feel short of breath and cough. • Too much thyroid hormone so you may feel anxious, angry, have trouble sleeping, feel weak, tremble, sweat, feel tired, have loose and watery stools • A potentially fatal condition that causes certain white blood cells to build up in and damage organs, including the bone marrow, liver, and spleen, and destroy other blood cells (hemophagocytic lymphohistiocytosis) • A condition that causes the body to stop making enough new blood cells for your body to work properly and can lead to tiredness, infections that last a long time, and easy bruising or bleeding (aplastic anemia)	• 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, 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

There are also side effects to the other drugs that you may receive in this study (cyclophosphamide, fludarabine, and IL-2). The side effects to treatment medications may result in life-threatening situations leading to intubation, dialysis, or other interventions. They may also be fatal.

Risks Associated with Cyclophosphamide, Fludarabine, and IL-2

Cyclophosphamide Side Effects

It is not known how often the following side effects may occur:		
• partial or total hair loss • mouth blisters/sores (possible difficulty swallowing) • nausea • vomiting • abdominal pain	• loss of appetite • diarrhea • problems with production of sperm and eggs • inability to have children • stopped menstrual cycle	• low blood counts (red, platelet, white) • bladder inflammation and bleeding (possible pain and/or urge to urinate) • infection

Cyclophosphamide may cause you to develop another type of cancer (such as bladder cancer, blood cancer, thyroid cancer, cancer of the bone marrow, and/or cancer that can start in the soft tissue, bone, or other tissue).

RARE, AND SERIOUS In 100 people receiving cyclophosphamide, 3 or fewer may have:		
• irregular heartbeat • build-up of fluid around the heart (possible heart failure) • inflammation of the heart and/or the tissue around the heart (possible chest pain and/or bleeding) • heart damage/failure, death of heart tissue, or other severe heart problems • blood clots in a vein (possible pain, swelling, and/or redness) • blood clots in an artery (possible organ damage such as stroke and/or heart attack) • brain injury that may be reversible (possible	• low blood levels of potassium (possible weakness) • low blood levels of sodium (possible headache, confusion, seizures, and/or coma) • hormonal deficiency that affects the body's ability to control blood pressure and react to stress • decreased supply of blood to the abdomen • digestive system bleeding • enlarged bowel (possible abdominal pain) • inflammation of the intestines (possible bleeding)	• hearing loss • breakdown of muscle tissue (possible kidney failure) • death of kidney tissue (possible kidney failure) • difficulty breathing • lung inflammation (possible difficulty breathing) • problems with blood carrying oxygen (possible blue skin) • lung damage due to blood clots • increased blood pressure in the lungs (possible difficulty breathing and/or heart failure) • multiorgan failure

headache, confusion, seizures, and/or vision loss) • dizziness • very severe blistering skin disease (with ulcers of the skin and digestive tract) • severe sunburn-like rash at site of previous radiation (called radiation recall) • wound healing problems • very severe blistering skin disease (loss of large portion of skin)	• inflammation of the pancreas (possible abdominal pain) • liver damage (possibly due to blood clots) • jaundice (yellowing of skin and/or eyes) • high blood levels of uric acid (possible painful joints and/or kidney failure) • ovarian scarring • urinary tract or bladder scarring • decreased testicle size and function • blood in the urine • blurry vision	• breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

Fludarabine Side Effects

COMMON, SOME MAY BE SERIOUS In 100 people receiving fludarabine, more than 20 and up to 100 may have:		
• fever • fatigue • pain • loss of appetite	• nausea • vomiting • low blood cell count (red, white, platelets)	• weakness • difficulty breathing • cough • infection

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving fludarabine, from 3 to 20 may have:		
• chest pain (possibly due to heart trouble) • heart failure • heart attack • fast and/or irregular heartbeat • blood clots in a vein (possible pain, swelling, and/or redness) • vein inflammation • swelling • chills • stroke • headache • difficulty sleeping • fatigue/lack of energy	• skin rash and/or itching • sweating • hair loss (partial or total) • high blood sugar (possible diabetes) • mouth blisters/sores (possible difficulty swallowing) • diarrhea • constipation • digestive system bleeding • gallstones • blood in the urine • difficult and/or painful urination	• inability to urinate • abnormal liver tests (possible liver damage) • abnormal sensation (such as pins and needles) • muscle pain • vision problems • hearing loss • swollen throat • sore throat • lung inflammation (possible difficulty breathing) • coughing up blood

RARE, AND SERIOUS In 100 people receiving fludarabine, 3 or fewer may have:		
• build-up of fluid in the tissue around the heart • weakness in wall of artery (possible serious bleeding complications) • multiple blood clots (possible organ dysfunction and/or failure) • bleeding in the brain • abnormal brain function (affecting balance and coordination) • progressive multifocal leukoencephalopathy (PML – a disease with brain damage that may likely result in paralysis and/or coma, which may be permanent, or death) • mental status change • temporary stroke symptoms • coma • seizure • abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure)	• painful blisters • very severe blistering skin disease (with ulcers of the skin and digestive tract) • very severe blistering skin disease (loss of large portion of skin) • allergic skin reaction • dehydration • abnormal pancreas tests • bladder inflammation with bleeding (possible pain and/or urge to urinate) • bone marrow failure due to abnormal tissue growth • increase in white blood cells • destruction of red blood cells and platelets due to abnormal antibodies • anemia due to destruction of red blood cells • condition causing increased bleeding and/or bruising • liver failure • nerve damage (possible numbness, pain, and/or loss of motor function) • nerve damage affecting the eye	• nerve damage (wrist weakness) • paralysis • loss of bone strength (possible broken bones) • blindness • inflammation of an eye nerve • high blood levels of uric acid (possible painful joints and/or kidney failure) • lung inflammation • lung damage (possible difficulty breathing) • bleeding in the lungs and/or airways • low oxygen level in the blood (possible lightheadedness) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage)

Fludarabine may rarely cause you to develop another type of cancer (such as skin cancer, cancer of the bone marrow, and blood cancer).

IL-2 Side Effects

COMMON, SOME MAY BE SERIOUS In 100 people receiving IL-2, more than 20 and up to 100 may have:		
• Fever • Chills • Fatigue • Lowered platelet and red blood cell levels that may require transfusions • Significant fluid retention causing weight gain (as much as 20 pounds)	• Low blood pressure • Increased heart rate • Low urine output • Swelling in your extremities • Fluid in your lungs that can require oxygen • Dry mouth • Nausea • Vomiting • Diarrhea • Rash	• Itching • Changes in skin or hair pigmentation, called vitiligo • Changes in mental status, including confusion, difficulty sleeping or vivid dreams; this can be severe and require sedation and monitoring in the ICU

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving IL-2, from 3 to 20 may have:		
• Decrease in thyroid function that may require daily thyroid hormone replacement • Abnormal kidney and liver function that can be severe	• Abnormal heartbeats or low blood pressure that may require treatment in the ICU	• Breathing problems which may need monitoring in ICU and insertion of a breathing tube

RARE, AND SERIOUS In 100 people receiving IL-2, 3 or fewer may have:		
• Bowel perforation (a hole) requiring longer hospitalization or surgery • Autoimmune disease, where your immune system attacks cells in organs of your body. Should this occur, you will be treated with steroids to stop the immune response	• Damage to the heart muscle or heart attack • Loss of blood flow to the extremities due to medicines used to treat very low blood pressure and shock. In one instance a patient had to have her lower arm amputated after treatment with these medicines	• IL-2 is mixed with human albumin which could cause an allergic reaction or potentially transmit viral infections, although we have not had this occur.

Risks Associated with Mesna

Mesna is used to reduce the risk of hemorrhagic cystitis (a condition that causes inflammation of the bladder and can result in serious bleeding in the urine and painful urination) in people who receive the chemotherapy drug cyclophosphamide.

The most common side effects of mesna are feeling sick (nausea), vomiting, constipation, low blood cell counts (white blood cells, red blood cells, and platelets), feeling tired, fever, decreased appetite (anorexia), stomach pain, hair loss (alopecia), and weakness or low energy.

Other more serious risks that you could face by taking mesna include the following:

- Hypersensitivity (allergic) reactions that may be severe and can include fever, low blood pressure that may make you feel dizzy or faint, fast heartbeat, kidney problems, low oxygen levels in your body, severe shortness of breath, hives, swelling of the face, tongue, mouth, or throat, feeling sick (nausea), vomiting, and joint and muscle pain.
- Drug rash that can affect both skin and mucosal membranes and may be severe. Symptoms can include hives, rash, reddening of the skin, itching, burning, swelling of the face, tongue, mouth, or throat, swelling around the eyes, and sores in the mouth.

Not all side effects of mesna are listed above. For more information about risks and side effects, ask your Study Doctor.

Other Risks

You may have side effects or discomfort from procedures like blood draws, tumor surgery, intravenous (IV) catheter, electrocardiogram (ECG), computed tomography (CT) scans, or magnetic resonance imaging (MRI). Please tell your Study Doctor right away if you do not feel well during any of the procedures.

Risk of blood draws

Bruising, swelling, and pain may occur at the site where you have blood taken. Rarely, fainting or infection at the site of the blood draw may also occur.

Risk of surgery

Surgery to remove a piece of tumor to create LN-144 has risks that include prolonged hospitalization, pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the surgery. An allergic reaction to the medication used to reduce pain may occur. A scar may form at the surgery site.

Risk of biopsy

Common side effects of a biopsy are a small amount of bleeding at the time of the procedure and local swelling, bruising, and pain at the biopsy site. The pain is usually minimal and can be treated with regular pain medications. Biopsy wounds usually heal with a very small, nearly unnoticeable scar, but sometimes a raised scar or visible lump may result. Infection of a biopsy site is unusual but may occur. A small scar may result at the biopsy site.

Risks of intravenous catheter

You will have an intravenous catheter (small tube placed in your vein) for infusion of chemotherapy, LN-144, and IL-2. Risks associated with the catheter insertion include swelling, bruising, redness, and infection at the point in which the catheter enters your skin.

Risk of ECG

An ECG is a painless, risk-free procedure. The ECG uses removable skin patches to monitor your heartbeat. The ECG procedure may cause mild discomfort while the skin patches (ECG leads) are being attached to and removed from the skin of your chest area. The ECG leads may also irritate your skin.

Risk of CT Scans and MRI

A CT scan, also called CT or computerized tomography, is an X-ray procedure where a high-speed computer is used to make multiple images or pictures of your body. CT scans create low levels of radiation; too much radiation over time has a small potential to cause cancer and other defects. However, the risk associated with an individual scan is small. The amount of radiation you may be exposed to each time is approximately the same as what you would receive as standard of care. The radiation exposure from CT scans has not been shown to cause harm to adult patients with advanced cancers.

You will be asked to lie still on a table and at times may have to hold your breath for a few seconds in order to avoid blurring the pictures. You may hear a slight buzzing, clicking, and/or whirring sounds as the CT scanner moves around your body.

Procedures such as CT scans may be used during this research study to examine your response to treatment. You may experience some discomfort, anxiety, or fatigue from lying inside the scanner. The contrast dye may cause you to get a metallic taste in your mouth, to feel a warm tingling and flushing sensation throughout your body for a few moments, and rarely cause nausea or vomiting. If you know that you have any possible allergies to drugs or foods (like shellfish), it is very important to tell the team performing these scans before you begin.

An MRI is a type of scan that uses magnetic fields to make a picture of the body and identify areas that could be suspicious of cancer. An MRI of your brain may be performed to rule out the spread of your cancer to the central nervous system or brain.

Some people cannot have an MRI because they have some type of metal in their body. For instance, if you have a heart pacemaker, artificial heart valves, metal implants such as metal ear implants, bullet pieces, chemotherapy, pain or insulin pumps or any other metal such as metal clips or rings, you cannot have an MRI.

During an MRI, you will lie in a small closed area inside a large magnetic tube. Some people are scared or anxious in small places (claustrophobic). The MRI scanner makes loud thumping noises while taking a measurement, so either ear plugs or specially designed headphones will be used to reduce the noise.

The MRI and CT scans have risks that include allergic reaction to the contrast dye. Your Study Doctor will discuss these risks and the procedure at length.

Unknown risks

There may be other risks and side effects that are not yet known and cannot be predicted. Therefore, it is important that you tell the Study Doctor or study staff right away about any changes in your health, not just the known risks and side effects listed above, even if you do not think they are side effects, because you are taking part in the study.

Pregnancy risks

Female patients

The effects of the study treatment on an unborn baby or a newborn baby are not known. Also, we do not know if the treatment can affect a woman's ovaries and possibly cause harm to a child should you become pregnant while you are taking the study treatment. Because of this, it is important that you are not pregnant or breast-feeding and do not become pregnant during the study. You must not take part in the study if you are pregnant or trying to become pregnant, or if you are breast-feeding.

For this reason, if you are able to become pregnant the study doctor will ask you to have a pregnancy test before the start of the study. Women are considered not able to become

pregnant only if they have been through menopause (change of life) and have not had a menstrual period for more than 1 year after menopause or if they have had sterilization surgery (tubes tied or a hysterectomy). The study staff will tell you if the pregnancy test shows that you are pregnant.

The study doctor will give you advice on the use of reliable birth control during the study. Acceptable methods to prevent pregnancy while you are taking part in this study are:

- Total abstinence (no sexual intercourse)
- Surgical sterilization including having your tubes tied (also called tubal ligation) or having your uterus or womb removed (also called hysterectomy) in women or a vasectomy in men
- Oral and injectable contraceptives (e.g. birth control pills, intrauterine devices [IUDs], or contraceptive implants)

If you do become pregnant, or suspect you are pregnant, while taking part in the study, you should tell your study doctor right away. Your study doctor will withdraw you from the study and advise you about further medical care if necessary. Your pregnancy will be monitored until you are no longer pregnant. The health of your newborn baby will also be monitored for 8 weeks following birth.

Male patients

The effects of the study treatment on an unborn child and on a newborn baby are not known. Also, we do not know if the treatment can affect a man's sperm and possibly cause harm to a child whom you father while you are taking the study treatment. If you are a male study participant and you have not had a vasectomy, you must agree to protect your female partner from becoming pregnant with the use of barrier methods (such as a condom), or total abstinence (no sexual intercourse) before and during the study and for 365 days after your last dose of all protocol-related therapy. If your partner becomes pregnant while you are on study, you must notify the study doctor right away.

7. What benefits can I expect from being in the study?

There may or may not be direct medical benefits as a result of your taking part in this study. However, your participation may help doctors to better understand the safety of the study treatment, LN-144, and how well it works to treat locally advanced stage III melanoma. This information may be helpful to treat other patients with locally advanced stage III melanoma in the future.

Your cancer may get smaller, stay the same, or grow during the study. Your medical condition may or may not improve as a result of taking the study treatment.

New information

While the study is ongoing, we will tell you as quickly as possible of any new information about LN-144 that may affect your decision to continue taking part in this study. In this case, you may be asked to sign a new informed consent form. The new information may also mean that you can no longer take part in this study.

8. What other choices do I have if I do not take part in the study?

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled.

You do not have to take part in this study for your illness to be treated.

If you decide not to take part in this study or the study is stopped, you may want to consider other treatments for your condition. Your Study Doctor will let you know about other treatments that are available to you as well as the important risks and benefits associated with them. Other treatments may include the following:

- Treatment with standard drugs and procedures such as chemotherapy, FDA-approved immunotherapy, or targeted therapy
- Other experimental treatments
- Other research studies
- Supportive care or no further therapy (comfort care)

You should discuss other alternative therapies and their benefits and risks with your Study Doctor.

If you complete the study after 3 years of your participation, you should follow up with your Study Doctor to discuss other treatment options available to you.

9. What are the costs of taking part in this study?

The study agents, LN-144, cyclophosphamide/fludarabine (chemotherapy drugs), and IL-2, will be supplied by the sponsor and will not be billed to you or your insurance company. Pembrolizumab infusion on Days -14, 28, and 70 will be supplied by the sponsor and will not be billed to you or your insurance company. You and/or your insurance company will not be billed for the cost of any tests or procedures that are required as part of this research study *and* are outside the standard of care for your condition.

You and/or your insurance company *will* need to pay for the costs of your regular medical care you get as part of the study, just as you would if you were getting the usual care for your condition. This includes:

- Pembrolizumab infusion during the maintenance phase of the trial (after Day 80 at weeks 6, 12 and 18, then every 3 months).
- Your tumor removal surgery after LN-144 and IL-2 treatment
- Your insurance co-payments, coinsurance, and/or deductibles.

Participating in this research study may lead to additional costs to you. In some cases, it is possible that your insurance company will not pay for these costs because you are taking part in a research study.

Talk to your insurance company and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this study. Also, find out if you need approval from your insurance company before you can take part in a research study.

Ask your doctor, nurse, or study coordinator for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance company.

10. Will I be paid for taking part in this study?

You will not be paid for taking part in this study

It is possible that this research project may result in developing treatments, devices, new drugs, or procedures that could be used for commercial profit. If this happens, you understand that you will not receive any financial payment or share in any commercial profit for the use of your information and biospecimens (such as blood or tissue samples) collected as part of this research.

11. What happens if I am injured because I took part in this study?

If you suffer an injury from participating in this study, you should notify the researcher or study doctor immediately, who will determine if you should obtain medical treatment at The Ohio State University Wexner Medical Center.

The cost for this treatment will be billed to you or your medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

12. What are my rights if I take part in this study?

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of research participants.

13. Will my de-identified information (and bio-specimens) be used or shared for future research?

Yes, they may be used or shared with other researchers without your additional informed consent.

OPTIONAL RESEARCH

There is an optional post-treatment biopsy of your tumor at Day 42. If you agree, leftover tumor tissue will be stored at Iovance Biotherapeutics (or its contractors) for use in research related to cancer. Before your samples are sent to Iovance Biotherapeutics (or its contractors) for banking, your name and any personal identifying information will be coded to protect your privacy. Iovance Biotherapeutics (or its contractors) will not have access to the codes that link the samples to your identity. OSU will not have oversight of any leftover samples that will be banked by Iovance Biotherapeutics (or its contractors) for additional research.

There are no benefits to you for taking part in the optional procedure. Future patients may benefit from what is learned. You may stop taking part at any time. There will be no cost to you for taking part in the optional procedure.

CONSENT / PERMISSION / AUTHORIZATION FOR OPTIONAL PROCEDURE

Do you agree to allow leftover tumor tissue to be stored by Iovance Biotherapeutics (or its contractors) for use in research related to cancer?

PLEASE CHECK ONE BOX

YES ☐ **NO ☐**

14. Will my study-related information be kept confidential?

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- The sponsor supporting the study, their agents or study monitors; and
- Your insurance company (if charges are billed to insurance).

If we find information that may significantly impacts your health, we **will** share it with you. For example, we may share limited test results from screening for certain transmissible infections (ie., HIV, Hepatitis B/C), and heart/lung function tests at the regular clinic or study follow-up visits. We will not share research results that may not impact your health (ie., the laboratory-based analysis of your immune system and tumor). Your personal identifiable information will be removed on these individual research results and will be published in aggregate with other patients who participate in this clinical trial.

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

15. HIPAA AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

I. What information may be used and given to others?

- Past and present medical records;
- Research records;
- Records about phone calls made as part of this research;
- Records about your study visits;
- Information that includes personal identifiers, such as your name, or a number associated with you as an individual;
- Information gathered for this research about:

HIV / AIDS
Hepatitis infection
Sexually transmitted diseases
Other reportable infectious diseases
Physical exams
Laboratory, x-ray, and other test results
Diaries and questionnaires
The diagnosis and treatment of a mental health condition

- Records about any study drug you received;

II. Who may use and give out information about you?

Researchers and study staff.

III. Who might get this information?

- The sponsor of this research. "Sponsor" means any persons or companies that are:
  - working for or with the sponsor; or
  - owned by the sponsor.
- Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information;
- If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic, or physician's office record;
- Others: Iovance Biotherapeutics Inc.

IV. Your information <u>may</u> be given to:

- The U.S. Food and Drug Administration (FDA), Department of Health and Human Services (DHHS) agencies, and other federal and state entities;
- Governmental agencies in other countries;
- Governmental agencies to whom certain diseases (reportable diseases) must be reported; and
- The Ohio State University units involved in managing and approving the research study including the Office of Research and the Office of Responsible Research Practices.

V. Why will this information be used and/or given to others?

- To do the research;
- To study the results; and
- To make sure that the research was done right.

VI. When will my permission end?

There is no date at which your permission ends. Your information will be used indefinitely. This is because the information used and created during the study may be analyzed for many years, and it is not possible to know when this will be complete.

VII. May I withdraw or revoke (cancel) my permission?

Yes. Your authorization will be good for the time period indicated above unless you change your mind and revoke it in writing. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the researchers. If you withdraw your permission, you will not be able to stay in this study. When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

VIII. What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study and receive research-related treatment. However, if you are being treated as a patient here, you will still be able to receive care.

IX. Is my health information protected after it has been given to others?

There is a risk that your information will be given to others without your permission. Any information that is shared may no longer be protected by federal privacy rules.

X. May I review or copy my information?

Signing this authorization also means that you may not be able to see or copy your study-related information until the study is completed.

16. Who can answer my questions about the study?

For study questions, concerns, or complaints, to withdraw consent and HIPAA authorization, or if you feel you have been harmed as a result of study participation, you may contact Dr. Richard Wu ***at (614) 293-0066 or 614-293-8000 (24 hours) or at the below address:***

460 W 10th Ave
5th Floor
Columbus, OH 43210

For questions related to your privacy rights under HIPAA or related to this research authorization, please contact ***HIPAA Privacy Manager, The Ohio State University Medical Center, Suite E2140, 600 Ackerman Road, Columbus, OH 43202 or at (614)293-4477***.

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact the Office of Responsible Research Practices at 1-800-678-6251.

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact Dr. Richard Wu at ***(614) 293-0066*** or ***614-293-8000 (24 hours).***

Signing the consent form

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this combined consent and HIPAA research authorization form**.**

Printed name of participant	**Signature of participant**
	AM/PM
	Date and time
Printed name of person authorized to consent for participant (when applicable)	**Signature of person authorized to consent for participant (when applicable)**
Relationship to the participant	**AM/PM** **Date and time**

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent	**Signature of person obtaining consent**
	AM/PM
	Date and time

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness	**Signature of witness**
	AM/PM
	Date and time
Printed name of witness	**Signature of witness**
	AM/PM
	Date and time