Informed Consent to Participate in Research and Authorization to Collect, Use, and Share Your Health Information
Moffitt Cancer Center/University of South Florida
**Information to Consider Before Taking Part in This Research Study**

Doctors and researchers at Moffitt Cancer Center study diseases and other health problems people with cancer may have. Our goal is to try to find better ways to help treat these health problems. To do this, we need the help of people who are willing to take part in a research study.

| | |
|---|---|
| **Study Title:** | **Phase 1b Study Using a Plasmid DNA Coding for Emm55 Streptococcal Antigen in Patients with Unresectable Stage III or Stage IV Cutaneous Melanoma** |
| **Protocol Number:** | **CM 2017-01** |
| **Sponsor:** | **Morphogenesis, Inc. (Morphogenesis)** |
| **Principal Investigator:** | **Joseph Markowitz, MD, PhD** |
| **(Study Doctor)** | **Medical Oncologist; Assistant Member-Department of Cutaneous Oncology** |
| **Telephone:** | **813-745-3437** |
| **(24 hour number)** | **800-456-3434** |
| **Address:** | **Moffitt McKinley Outpatient Center**<br>**10920 N. McKinley Drive, Tampa, FL 33612**<br>**(813) 745-4673** |

**Why are you being asked to be in this research study?**

You are being asked to be in this study because you have been diagnosed with melanoma that cannot be cured with surgery. You have also met the requirements to participate in the study.

If you are pregnant, nursing an infant, or plan to become pregnant during this study, you may not be in this study.

How many people will take part in this study?

About 8 subjects are expected to participate in this study here at Moffitt Cancer Center.

**What is the reason for doing this research study?**

The purpose of this study is to test the safety of a new drug for melanoma as a potential treatment in patients diagnosed with this disease. The drug product is, IFx-Hu2.0 (genetic material called plasmid DNA that will be injected). This is a "First-in-human" study. Possible side-effects listed in this consent form are based on other clinical trials of similar products and results from IFx-Hu2.0 studies in animals. Due to the fact that humans and animals may respond differently to agents like this, animal studies may not reveal all of the potential side effects in humans. The value of IFx-Hu2.0 as a medicine has not yet been proven and it is not yet approved by the FDA.

In general, medicines called vaccines (IFx-Hu2.0 is a vaccine) help the body's immune system to recognize and kill living things such as bacteria that should not be in the human body. A vaccine that alerts the immune system to the presence of cancer cells could lead to the immune system being able to target and kill those cancer cells.

This trial is a new application of plasmid DNA vaccines to treat cancer. The IFx-Hu2.0 vaccine consists of plasmid DNA that contains genetic code for the Emm55 protein. The Emm55 protein is very capable of provoking or producing an immune response. The Emm55 protein comes from a type of bacteria called, Group A Streptococci. IFx-Hu2.0 will be injected via syringe into a melanoma lesion which has a high number of tumor cells. These melanoma cells will take up the plasmid DNA. When the plasmid DNA is in the melanoma cell, the Emm55 protein will be produced. The goal is that this will start an immune response to kill cancer cells.

**What will be done during this research study?**

If you participate in this study you will be given a single dose of the experimental vaccine, IFx-Hu2.0, injected into up to three separate lesions. You will then be evaluated 4 weeks later and the findings compared to your initial, baseline, evaluation. You will be in the trial for one month unless you qualify for more therapy as described below. If the principal investigator believes that there is a significant safety concern, they may terminate the therapy without your consent. We are not predicting this to happen, but this can include a scenario where the immune system is

stimulated too much and you may require medications to reduce the immune response. If you decide to withdraw from the research study, this will be handled at the early termination visit.

A camera may be used to photograph your lesions on the skin. We are requesting that you allow us to take a few additional pieces of tissue to study the how the study drug works. If you have a good response to therapy, you will be allowed to continue the therapy. If you are a woman of childbearing years you will receive a urine pregnancy test before each dose.

Male participants who are able to father children and female patients who are able to have children must use effective contraception through study treatment and for 30 days after the study treatment is stopped.

If you are currently pregnant, planning to become pregnant, or breastfeeding a child, do not join this study. If you are a male whose partner is currently pregnant or if you plan to father a child, do not join this study.

The study doctor will talk to you about the types of birth control that you can use while taking part in this study. They will help you select birth control that is the best choice for you. At least one form of barrier contraception is mandatory. The study doctor will instruct you in correct use of your selected birth control methods. They will review your responsibility to use this birth control consistently and correctly at each visit.

Birth control methods, even when used properly, are not perfect. If you or your partner becomes pregnant during the study, or you want to stop using birth control during the study, you should tell the study doctor immediately. Your study doctor will remove you from the study if you stop using birth control or you become pregnant.

**Screening Visit (Day -36 to -1)**

- Obtain informed consent of potential participant confirmed by signature on study informed consent form.
- Review the requirements to go on the trial with the patient
- Review medical history.
- Review medications history
- Perform medical examinations
- Obtain imaging exams to see where in your body the melanoma is located. This can include CT and/or PET/CT. Photographs may also be utilized for “skin only” melanoma.
- Electrocardiogram (ECG)
- Collect blood/urine/where feasible, research study biopsy as determined by the principal investigator may be obtained on the first and subsequent and subsequent treatment cycles. In the setting of known melanoma, tumor tissue that has been collected previously may be utilized to confirm the diagnosis (Moffitt or from external source). Research biopsies will

be obtained using a punch or shave biopsy technique. Genetic or other study materials may be stored for future use for correlative experiments in this trial.

- Measurement of how much activity you can perform (ECOG Performance Status.)
- Assessment and recording of Tumor Burden (lesion measurements).
- Provide general study procedures and instructions for clinical visits.

**Enrollment/Baseline**

Enrollment/Baseline Visit (Visit 1, Day 0)

- Obtain demographic information, medical history, medication history, alcohol and tobacco use history.
- Record vital signs, results of examinations, other assessments.
- Collect blood/urine routine laboratories and 40 mL of blood will be collected for research purposes Research study biopsy for histology and immune response assays may be collected at the screening visit or the baseline visit
- Administer the study treatment.
- Determine your Performance Status
- Assessment and recording of Tumor Burden (lesion measurements).
- Observation and recording of any problems that you are having while on this study as defined by the regulatory manual (CTCAE V5.0)

**Final Study Visit**

Final Study Visit (Week 4 Day 28 +/-7 business days or 21+/- 7 business days after the last dose)

- Record side effects (adverse events) as reported by participant or observed by investigator
- Record vital signs, results of physical examination
- Collect blood/urine
- Record participant's adherence to treatment regimen
- Collect 40 mL of peripheral blood for research purposes
- Tumor sample biopsy of injected lesion for research studies
- Biopsy of non-target lesion (if applicable)
- Assessment and recording of Performance Status
- Assessment and recording of Tumor Burden (lesion measurements).
- Observation and recording of any problems that you are having while on this study as defined by the regulatory manual (CTCAE V5.0)
- CT as clinically indicated and/or PET scan

**Early Termination Visit**

- Record adverse events as reported by you the clinical trial participant or as seen by the study staff. Record vital signs, results of physical examination
- Collect blood/urine
- Record participant's adherence to treatment regimen
- Tumor sample biopsy and research blood samples
- Measure and record ECOG Performance Status
- Assessment and recording of Tumor Burden (lesion measurements).
- Observation and recording of any problems that you are having while on this study as defined by the regulatory manual (CTCAE V5.0)
- With patient consent may obtain two biopsies of the skin.

**Unscheduled Visit**

- Record adverse events as reported by you the clinical trial participant or as seen by the study staff. as
- Record vital signs, results of physical examination
- Collect blood/urine Record participant's adherence to treatment regimen
- Observation and recording of any problems that you are having while on this study as defined by the regulatory manual (CTCAE V5.0)
- Assessment and recording of Performance Status

You have the option to continue treatment every three weeks at the investigator's discretion in consultation with the sponsor.

**Long Term Follow-Up**

To occur on 11/16/2020 (± 4 weeks):

- Review of medical record
- Collection of further melanoma treatments and results of those treatments

**What are the possible risks of being in this research study?**

Side effects have not been detected in pre-clinical studies, there is a possibility of autoimmunity (i.e. immune reaction against one's own tissues – skin, thyroid, etc.) Patients receiving other cancer vaccine therapies have experienced reactions including mild fever, skin reactions, sweats and chills, shortness of breath and low blood pressure. Although we are not expecting life threatening complications, we will monitor for life threatening allergic reactions, high fever for more than 72 hours, heart issues, and any other side effects that you may bring to our attention. The safety and tolerability of IFx-Hu2.0 will be monitored in real-time by study investigators by means of adverse event reporting and clinical reports of laboratory and clinical data. Guidelines

for toxicity used by the National Cancer Institute will be followed to assign a level or severity to any serious adverse event.

It is possible that the medicines used in this study could injure a fetus if you, or your partner, becomes pregnant while taking them. You have already been told what is known about this possibility, and you are encouraged to ask further questions.

You may want to discuss this with others before you agree to take part in this study. If you wish, we will arrange for a doctor, nurse, or counselor who is not part of this study to discuss the potential risks and benefits with you and anyone else you want to have present.

Because of the potential risks, you, or your partner, must not become pregnant while you are participating in this study. Women must have a negative pregnancy test before entering the study.

If you are sexually active and can get pregnant, or can get your partner pregnant, you must use TWO appropriate method(s) of birth control every time you have sex, or you must not have sex. Acceptable methods of contraception are condoms with contraceptive foam, oral, implantable or injectable contraceptives, contraceptive patch, intrauterine device, diaphragm with spermicidal gel, or a
sexual partner who is surgically sterilized or post-menopausal.

Because of the nature of this research, methods of natural family planning are not, by themselves, sufficiently reliable to avoid pregnancy.

You will need to continue to avoid pregnancy for 6 months after finishing the research.

By signing this and being in the study, you are agreeing to not get pregnant while you are on the study and for 6 months after. Should you become pregnant while on this study, you should immediately notify the study personnel. The investigator will assist you in finding appropriate medical care. The investigator also may ask to be allowed to continue getting information about your pregnancy. You can refuse to provide this information.

It is possible that other rare side effects could occur which are not described in this consent form. It is also possible that you could have a side effect that has not occurred before.

**What are the possible benefits to you?**

You are not expected to get any benefit from being in this research study.

This is a safety study and no clinical benefit is expected; the goal is to test for the safety of this approach and evaluate any potential immune response to this vaccine.

It is unusual for subjects in a Phase I study like this to receive health benefits from an investigational vaccine.

Patients receiving the vaccine may respond to the therapy by producing an immune response to the Emm55 antigen and to their own tumor cells. This may result in gradual reduction of your tumor burden and a decrease in melanoma-related symptoms.

**What are the possible benefits to other people?**

Your participation in the study will contribute to information about the IFx-Hu2.0 vaccine and may benefit other patients in the future.

## WHAT ARE MY ALTERNATIVES TO BEING IN THIS STUDY?

You do not have to be in this study to get help for your melanoma. The study doctor will talk to you about other things you can do for melanoma including the important risks and benefits. Your participation in this study is voluntary. You can decide not to be in the study and you can change your mind about being in the study at any time. There will be no penalty to you, and you won't lose any benefits. Your regular medical care at this study center will not change if you decide not to be in the study.

Alternative treatments for cancer include:

- Getting treatment or care for your cancer without being in a study
- Treatment with chemotherapy. Prior to going on this study you should have already considered BRAF/MEK therapies or anti-PD-1 therapy. Please ask your doctor about this if you have questions.
- No additional treatment to stop the cancer growth and focusing instead on controlling your symptoms (comfort care)
- Participation in another research study

**Will you be given any important information during the study?**

You will be informed promptly if the research team gets any new information during this research study that may affect whether you would want to continue being in the study.

## WILL IT COST ANYTHING TO BE IN THIS STUDY?

You and/or your insurance company will be financially responsible for hospital inpatient, outpatient and follow-up visits that would normally or routinely occur in the management of your disease. Inpatient and outpatient visits could include charges for treatments, medications, physician visits, laboratory tests and procedures. You and /or your insurance company will be responsible for paying for the charges which are considered routine, since you would have received these services even if you were not participating in this study. You will be responsible for any costs not covered by your insurance company, including deductibles, co-payments and all out-of-pocket expenses. Before you agree to be in this study, you should contact your health insurer to see if your plan will cover the costs required as part of your participation.

You and/or your insurance company will not be responsible for paying for study related items and services that are specifically required for this research study and are not considered part of the routine management of your disease, if these procedures are performed at Moffitt Cancer Center.

During your participation in this study, Morphogenesis will be responsible for providing the study drug, IFx-Hu2.0, at no additional charge to you. You and/or your insurance company will be responsible for the charges related to the administration of the study drugs.

You and/or your insurance company will be responsible for the drug Keytruda® (pembrolizumab) that is commercially available. You and/or your insurance company will be responsible for the charges related to the administration of the commercially available drugs.

If you would like more information on the costs of being on this study or have other insurance related questions, then please let your clinical trial coordinator know or contact our Business Office at 813-745-8422.

## WHAT IF I GET HURT OR SICK WHILE I AM IN THIS STUDY?

**If you need emergency care:**

- Call 911 or go to your nearest emergency room right away. Moffitt Cancer Center does not have an emergency room or the facilities to provide emergency care.

**If you do NOT need emergency care:**

- Call or go to your regular doctor. It is important that you tell your regular doctor that you are participating in a research study. If possible, take a copy of this consent form with you when you go.

If you experience a side effect or a change in the way that you feel, call the study doctor at the telephone number listed on the first page of this form.

If you are injured by or become ill from participating in this study, medical treatment is available at Moffitt Cancer Center, or you may seek treatment elsewhere.

Morphogenesis will reimburse your reasonable and necessary medical expenses for diagnosis and treatment of a research-related illness or injury through Moffitt Cancer Center or other another facility if the injury or illness;

- Is a direct result of IFx-Hu2.0 (the drug being tested);
- Is not a medical condition that you had when you started the study; and
- Is not the direct result of proven negligence of Moffitt Cancer Center

Morphogenesis does not plan to provide any other form of compensation to you for any illness or injury resulting from this study.

By signing this informed consent and research authorization form, you have not given up any legal rights to seek compensation for injuries from the sponsor**.**

## MOFFITT CANCER CENTER INJURY STATEMENT

If you believe you have been injured as a result of your participation in this study or if you have questions about your rights as a person who is taking part in a research study, you may call the Moffitt Cancer Center Risk Manager at 813-745-4219. Florida law (Statute 768.28) limits the liability of Moffitt Cancer Center. Moffitt Cancer Center cannot pay for lost wages, disability, or discomfort. A copy of this statute is available upon request at 813-745-1869. This statute provides that damages are available only to the extent that negligent conduct of a Moffitt Cancer Center employee caused your injuries, and are limited by law. The Moffitt Cancer Center and investigators have made no provision for monetary compensation in the event of physical illness or injury resulting from this study.

## HOW WILL MY INFORMATION BE KEPT CONFIDENTIAL?

We understand that information about you and your health is personal, and we are committed to protecting the privacy of that information. Because of this commitment and because of federal law, we must obtain your written authorization before we use or disclose your information for this study.

By signing this form, you are permitting researchers at Moffitt Cancer Center to use personal health information for research purposes within its organized health care arrangements. You are also allowing the Moffitt Cancer Center to disclose your personal health information to outside organizations or individuals that participate in this study. We may publish what we find out from this study. If we do, we will not let anyone know your name. We will not publish anything that would directly let people know who you are.

## WHO WILL DISCLOSE, RECEIVE, AND/OR USE YOUR INFORMATION?

Your records are confidential and they will be kept in a secure environment and protected to the full extent of the law.

To do this research, the following people and/or organization(s) will be allowed to disclose, use, and receive your information, but they may only use and disclose the information to the other parties on this list, to you or your personal representative, or as permitted by law:

- Every research site for this study, including the Moffitt Cancer Center, and each site's study team, research staff and medical staff
- Any person who provides services or oversight responsibilities in connection with this study
- Every member of the Moffitt Cancer Center workforce who provides services in connection with this study

- The person who is responsible for the study nationwide or worldwide (study chairperson)
- Any laboratories, individuals, and organizations that use your health information in connection with this study
- The study sponsor; Morphogenesis
- Any federal, state, or local governmental agency that regulates the study (such as the U.S. Food and Drug Administration (FDA) and Florida Department of Health (FDH). The U.S. Department of Health & Human Services (DHHS), Office for Human Research Protections (OHRP)
- Other government agencies in this or other countries
- The designated Protocol Review and Monitoring Committees, Institutional Review Boards, Privacy Boards, Data and Safety Monitoring Board and their related staff that have oversight responsibilities for this study
- The National Cancer Institute in evaluating the ongoing research of the Moffitt Cancer Center as a Comprehensive Cancer Center

The organizations and people listed above may employ or pay various consultants and companies to help them understand, analyze and conduct this study. All of these people may not be known now, but if you would like to have more specific information about this at any time during the study, you may ask the study doctor and your questions will be answered.

Moffitt Cancer Center cannot guarantee the privacy of your information, or block further use or distribution, after the information has left the Moffitt Cancer Center. Others listed above may further disclose your information, and it may no longer be covered by federal privacy regulations. If all information that does or can identify you is removed from your records, the remaining information will

no longer be subject to this authorization and may be used or shared for other purposes. You might have the right to see and copy your health records related to this research. You might not be able to see or copy some of your records until after all participants finish the study. If it is necessary for your care, your records will be provided to you or your regular doctor.

Genetic Information Nondiscrimination Act (GINA)
A new Federal law, called 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.

All health insurance companies, group health plans and employers as outlined above must follow this law. Please note that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

## WHAT INFORMATION WILL BE USED OR DISCLOSED?

By signing below, you authorize the use and disclosure of your entire study record and any medical or other records held by Moffitt Cancer Center, including, but not limited to, HIV/AIDS, mental health, substance abuse or genetic information. The purpose for the uses and disclosures you are authorizing is to conduct the study explained to you during the informed consent and research authorization process and to ensure that the information relating to that study is available to all parties who may need it for research purposes.

Your authorization to use your health information will never expire unless and until you expressly revoke it in writing to the study doctor listed on the first page of this form.

Any data collected before your letter will continue to be used as necessary to preserve the integrity of the study, however no additional information will be collected after you withdraw your authorization.

You will receive a signed and dated copy of this form.

## GETTING ANSWERS TO YOUR QUESTIONS OR CONCERNS ABOUT THE STUDY

You can ask questions about this consent form or the study (before you decide to start the study, at any time during the study, or after completion of the study). Questions may include:

- Who to contact in the case of a research-related injury or illness;
- Payment or compensation for being in the study, if any;
- Your responsibilities as a study participant;
- Eligibility to participate in the research;
- The study doctor's or study site's decision to exclude you from participation;
- Results of tests and/or procedures;
- Other questions, concerns, or complaints

***Contact the study doctor or study staff <u>listed on the first page of this form</u> with any questions, concerns or complaints.***

## GETTING ANSWERS TO YOUR QUESTIONS ABOUT YOUR RIGHTS AS A RESEARCH PARTICIPANT

This study has been reviewed by an Institutional Review Board (IRB). This Committee reviewed this study to help ensure that your rights and welfare are protected and that this study is carried out in an ethical manner.

If you have questions about your rights, complaints, or issues as a person taking part in this study, call the Division of Research Integrity and Compliance-Institutional Review Board (IRB) of the University of South Florida at (813) 974-5638

**WHERE CAN I GET MORE INFORMATION?**

You may call the National Cancer Institute's (NCI) Information Service at:

- 1-800-4-CANCER (1-800-422-6237)

Visit the NCI's Websites at:

- CancerTrials: comprehensive clinical trial information at: http://cancertrials.nci.nih.gov
- CancerNet: accurate cancer information including PDQ at: http://cancernet.nci.nih.gov

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.

**STATEMENT OF CONSENT**

I have read this form and its contents were explained to me. I agree to be in this research study for the purposes listed above. All of my questions were answered to my satisfaction. I will receive a signed and dated copy of this form for my records.

_____

Printed Name of Participant

_____ _____

Signature of Participant Date

**STATEMENT OF PERSON OBTAINING INFORMED CONSENT/RESEARCH AUTHORIZATION**

I attest that the participant named above had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to be in this study.

_____

Printed Name of Person Explaining Consent

_____ _____

Signature of Person Explaining Consent Date