PRINCIPAL INVESTIGATOR: Raffit Hassan, M.D.

STUDY TITLE: A Phase I Study of the Mesothelin-Targeted Immunotoxin LMB-100 with or without *Nab*-Paclitaxel (Abraxane) in Patients with Malignant Mesothelioma

STUDY SITE: NIH Clinical Center

Cohort: Part A -LMB-100 monotherapy

Consent Version: 03/01/2020

WHO DO YOU CONTACT ABOUT THIS STUDY?

Raffit Hassan, M.D. by phone at 240-760-6232 or email raffit.hassan@nih.gov

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

If the individual being asked to participate in this research study is not able to give consent to be in this study, you are being asked to give permission for this person as their decision-maker. The term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research, throughout the remainder of this document.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

In this study, we will determine a safe dose of LMB-100 in patients with advanced mesothelioma with or without *nab*-paclitaxel. LMB-100 is an investigational agent, meaning that it has not been approved by the US Food and Drug Administration. It is a type of manufactured protein which is similar to protein normally produced by your body in response to a specific foreign substance. LMB-100 is attracted to the mesothelin protein, which is present in a lot of different tumors,

including mesothelioma, but is found in only a very small number of normal tissues. After binding to the mesothelin on tumors, LMB-100 can then attack and kill cancer cells. *Nab*-paclitaxel is an FDA approved agent used in the treatment of breast cancer, non-small cell lung cancer and pancreatic cancer. Its use in this study is investigational as it has not been approved in the treatment of mesothelioma. Part A of the study included two groups of patients (Arms A1 and A2) who were assigned to receive LMB-100 alone. In part B, two other groups (Arms B1 and B2) will be assigned to receive LMB-100 with *nab*-paclitaxel. You are participating in either Arm A1 or A2 depending on when you were enrolled on the study..

WHY ARE YOU BEING ASKED TO TAKE PART IN THIS STUDY?

You are being asked to take part in this study because you have pleural or peritoneal mesothelioma that has not responded to prior platinum based therapy.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 34 participants will be enrolled in the study, 10 in part A and the remainder in part B.

DESCRIPTION OF RESEARCH STUDY

The first 3 participants were enrolled in the phase 1 portion of part A (Arm A1) at the highest dose of LMB-100 that we will test. As there were intolerable side effects in more than 1 subject at this dose, the next lowest dose was given in the next 7 subjects enrolled and the 3 original subjects received the lower dose during their next treatment cycles. Of these 10 participants; 9 had stable disease, meaning the tumor did not change in size, while in 1 subject the tumors grew. There were no intolerable side effects at this dose. No additional patients will be enrolled in part A, but you will continue to receive LMB-100 alone if your disease has not worsened. Please note that based on the information from ongoing clinical trials of LMB-100, giving LMB-100 alone for more than 2 cycles provides no additional clinical benefit as we are unable to detect LMB-100 in the majority of participants beyond cycle 2.

You will receive LMB-100 through an IV catheter (a tube inserted in a vein, usually in your arm) on day 1, day 3 and day 5 of each 21-day cycle. You will receive LMB-100 for up to 4 cycles or until your disease worsens or you have intolerable side effects, whichever happens first. We will continue to follow you after you have finished taking the study drug to keep track of your disease status (progression), your survival status or whether you have taken any additional cancer therapy. The specific procedures you will have are described below.

WHAT WILL HAPPEN IF YOU TAKE PART IN THIS RESEARCH STUDY?

Before you begin the study

Before beginning the study, you will need to undergo tests and/or procedures to help your doctor verify whether you can participate. This is called screening. Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, there are some extra procedures that you will need to have if you take part in this study. If you have already undergone some of these examinations very recently, your doctor may decide not to repeat them. Briefly, these tests, which are performed under a separate consent, include:

- Confirmation of diagnosis (You must provide a sample tumor tissue for an evaluation from the NCI Laboratory of Pathology. The tissue may be from a previous surgery, biopsy or

collection from a tumor effusion (fluid around the tumor). If none is available, we will ask you to have a biopsy or a collection of effusion material to provide a fresh sample). Please see page 7, Tumor Biopsies and Effusions for a description of the procedure.

- Medical history and physical examination
- Routine blood and urine tests including pregnancy test in women who can have children. Pregnant women will not be allowed on study.
- Scans and x-rays
- Electrocardiogram (ECG)
- Echocardiogram
- Tests for viruses (hepatitis and HIV)

During the study

Once it is determined that you are eligible and you have signed the consent for the study, you will receive IV infusions of LMB-100 as described above. Each infusion will last about 30 minutes, but it might take longer if your study doctor decides it is needed for your safety. You will be monitored for side effects for 2 hours after the first infusion, and for 30 minutes after all other infusions if no side effects occurred previously. We will give you standard pre-medications that include an antihistamine (such a Benadryl), acetaminophen (Tylenol), ranitidine (Zantac) and dexamethasone, a steroid to help prevent infusion related side effects.

While you are taking study medication, we will perform a number of tests and examinations for safety and to test the effect of the study therapy.

These include routine blood and urine tests that will be done 4 – 5 times per cycle, a chest X-ray on day 1 of each cycle, scans that will be performed approximately every 6 weeks, and ECGs that will be done just before each infusion.

We will also perform tests for research studies to find out how your body handles the drug (PKs), the types of immune cells present in your disease, how your body reacts to the drug and how certain side effects of the LMB-100 might be caused. Most of the sampling for these research tests will be done before your first dose of study drug, on the days you take the study drug (just before or just after you get the study drug) or at the end of treatment. In addition, a blood sample will be collected at the end of cycle 2 and on day 8 of each cycle. Exceptions to this are:

- PK studies on days 1 and 5 of cycle 1 and on day 1of cycle 2. These samples will be drawn before your infusion and periodically for up to 6 hours after the start of infusion.

- Optional biopsies which may be collected before the first dose of LMB-100 (if you have not given a biopsy at screening) and after you have completed two cycles of therapy. The biopsies to be performed are exclusively for research purposes and will not benefit you. It might help other people in the future. You will be given the opportunity to decide whether you want to have these sample collected at the time of each biopsy. All tissue will be reviewed by the NCI Laboratory of Pathology.

When you are finished taking the drugs

Approximately 4 – 6 weeks after you have had your last dose of study drug, you will be asked to return to the NIH for a follow up visit to have the following tests:

- Medical history and physical exam
- Routine blood and urine tests
- Scans if your disease has not worsened since the beginning of the study
- ECG

If after this visit, your disease remains stable or improves, you will continue to be scanned every 6 weeks until your disease worsens.

About once a year, regardless of whether your disease has gotten worse, we will contact you or your physician by telephone to ask about any other cancer therapies you may have started and about your survival status.

BIRTH CONTROL

If you are a woman who is breast feeding or pregnant, you may not take part in the study because we don't know how this medicine would affect your baby or your unborn child. If you are a woman who can become pregnant, or are the partner of a woman who can become pregnant, you will need to practice an effective form of birth control before starting study treatment, during study treatment, and for 3 months after you finish study. In addition, male subjects should not donate sperm during the study and for 3 months after the last dose of study therapy. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once.

Effective forms of birth control include:

- abstinence
- intrauterine device (IUD)
- hormonal [birth control pills, injections, or implants]
- tubal ligation
- vasectomy

RISKS OR DISCOMFORTS OF PARTICIPATION

Risks and Possible Undesirable Effects of LMB-100

Prior to this study LMB-100 has only been given to 15 subjects; therefore, we do not know all of the possible side effects. However, below is a list of the most common and most serious side effects occurring on the earlier study, some occurring at higher doses than will be used in this study.

The most common side effects (some were serious) were:

- Low levels of the blood protein albumin which may lead to swelling, muscle weakness or loss of appetite

- Tiredness
- Swelling of the arms and legs
- Nausea
- Fever
- Decreased appetite
- Shortness of breath
- Pain in muscles

Less common, but serious side effects included:

- Fluid in the organs which may cause low blood pressure, shortness of breath, swelling of ankles
- Abnormal heartbeat
- Reactions during or following the infusion of the drug which may cause fever, chills, rash or low blood pressure
- Pain in joints
- Kidney damage which may cause swelling, may require dialysis

Other possible side effects

Other possible side effects discussed below are based on side effects that occurred when testing a similar agent, SS1P and in animal studies of LMB-100. It is possible that there may be other unexpected side-effects that occur in addition to those listed below.

LMB-100 may cause inflammation to membranes causing chest pain, shortness of breath, low blood pressure, and heart failure. In animals, some mild kidney toxicity was seen, characterized by increased enzymes and protein in the urine. This will be checked for with regular blood and urine tests.

As with other drugs similar to LMB-100, there is a chance that the drug could cause the body to produce an unwanted response called 'Anti-drug antibodies' (ADAs). These might not cause problems however there is a chance they could lead to a severe anti-drug response in the body. ADA levels will be measured during the study to monitor any changes.

There may also be pain and swelling at the infusion site.

It is important that you contact your doctor as soon as you experience any side effects whether you think the treatment has caused them or not. You must also tell your doctor if you have started any new medication or had a change to your existing medication. This includes medications available without a prescription (over the counter) and alternative medicines. If you have any questions or concerns about any of the information provided above, about the possible side effects of treatment, or the possible consequences of treatment for those side effects, please ask the principal investigator or the research staff for more information.

The most important symptoms you need to report to your doctor <u>immediately</u> are:

- possible infusion or allergic reactions (symptoms that start during or within a few hours of the infusion, e.g., wheezing, tightness in the throat or chest, rash, and facial swelling)
- chest pain
- shortness of breath
- palpitations (fast heart beat)
- bleeding and high fever
- impaired brain function (e.g., dizziness, blurred vision, confusion)

If you experience any severe or dangerous side effect, you should:

1. Seek professional medical help immediately.
2. Call your study doctor.
3. If necessary, go to the nearest emergency room.

Risks from pre-medications

Acetaminophen

Acetaminophen is considered to be safe and effective in the recommended doses. However, when taken incorrectly acetaminophen can cause liver damage. Your risk of liver damage may be increased if you drink more than three alcoholic drinks every day, take more than the recommended dose (overdose), or if you take any additional drugs that also contain acetaminophen at the same time.

Diphenhydramine

Drowsiness, dizziness, constipation, stomach upset, blurred vision, or dry mouth/nose/throat may occur when taking diphenhydramine.

Ranitidine:

It can cause constipation, diarrhea, headache, nausea or upset stomach. Rare serious side effects include severe allergic reaction with rash, hives, itching, difficulty breathing; confusion, dark urine, depression, fast or slow heartbeat, unusual bruising or bleeding, yellowing of the eyes or skin (indicating liver damage).

Dexamethasone:

Stomach upset, headache, dizziness, changes in your period, trouble sleeping, increased appetite, or weight gain may occur. Rarely patients using dexamethasone have experienced increased infection, bone/joint pain, thirst, increased urination, irregular heartbeat, eye pain, vision problems, black stools, vomit that looks like coffee grounds, puffy face, swelling of the feet and ankles, pain/redness/swelling of the arms or legs, tiredness, mood changes, unusual hair/skin growth, muscle cramps, weakness, easy bruising/bleeding, slow wound healing, thinning skin and seizures.

Risks from Study Procedures

The following study procedures and treatments may have risks and cause discomfort while you participate on this study:

Blood draws

There is the risk of slight pain, bruising or infection when your blood is drawn. Drawing blood may cause some people to faint.

ECGs

The glue used to keep the electrodes in place during the ECG may irritate your skin and cause redness.

Tumor Biopsies and Effusions

Tumor biopsies and tumor effusions: local anesthesia of the skin will be given prior to any tumor biopsy or effusion collection, in order to prevent painful sensations. However, you may still experience pain or discomfort at the biopsy site. Irritation, redness, swelling and/or bleeding may also occur. There is a risk of abnormal healing, fever, infection or of an allergic reaction to the anesthetic agent used to anesthetize the skin at the biopsy site. Once the sample has been obtained, a stitch may be used to close the wound and facilitate healing.

In some cases, we may use CT scans to help guide us during your biopsy. This introduces the added risk of research radiation. This research study may involve exposure to radiation from up to 2 CT guided tumor biopsies**.** This radiation exposure is not required for your medical care and is for research purposes only. The amount of radiation you will receive in this study is 1.5 rem which is below the guideline of 5 rem per year allowed for research subjects by the NIH Radiation Safety Committee. The average person in the United States receives a radiation exposure of 0.3 rem per year from natural sources, such as the sun, outer space, and the earth's air and soil. If you would like more information about radiation, please ask the investigator for a copy of the pamphlet, An Introduction to Radiation for NIH Research Subjects.

While there is no direct evidence that the amount of exposure received from participating in this study is harmful, there is indirect evidence it may not be completely safe. There may be a very slight increase in the risk of cancer.

Please tell your doctor if you have had any radiation exposure in the past year, either from other research studies or from medical tests or care, so we can make sure that you will not receive too much radiation. Radiation exposure includes x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body.

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

The aim of this study is to find a safe dose for this experimental treatment. We do not know if you will receive personal, medical benefit from taking part in this study. These potential benefits could include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer. Because there is not much information about the drug's effect on your cancer, we do

not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?

Instead of being in this study, you have these options**:**

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Please talk to your doctor about these and other options.

STOPPING THERAPY

Your doctor may decide to stop your therapy for the following reasons:

- if he/she believes that it is in your best interest
- if your disease comes back during treatment
- if you become pregnant
- if you have side effects from the treatment that your doctor thinks are too severe
- if new information shows that another treatment would be better for you

In this case, you will be informed of the reason therapy is being stopped.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to collaborators or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases can**not** be recalled and destroyed.

CONFLICT OF INTEREST

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a Protocol Review Guide. You may ask your research team for a copy of the Protocol Review Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines but they do not need to report their personal finances to the NIH.

Members of the research team working on this study may have up to $15,000 of stock in the companies that make products used in this study. This is allowed under federal rules and is not a conflict of interest.

The National Institutes of Health and the research team for this study have developed a drug being used in this study. This means it is possible that the results of this study could lead to payments to NIH scientists and to the NIH. By law, government scientists are required to receive such payments for their inventions. You will not receive any money from the development of LMB-100.

Celgene is providing the *nab*-paclitaxel for this study to NIH without charge. No NIH employee involved in this study receives any payment or other benefits from Celgene.

USE OF SPECIMENS AND DATA FOR FUTURE RESEARCH

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that it may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. The amount and form

of these payments are determined by the NCI Travel and Lodging Reimbursement Policy. You will be given a summary of the policy which provides more information.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- If some tests and procedures are performed outside the NIH Clinical Center, you may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- Qualified representatives from Celgene, the pharmaceutical company who produces nab-paclitaxel

When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Raffit Hassan, M.D., raffit.hassan@nih.gov, 240-760-6232. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR	Print Name of LAR	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only: This section is only required if you are doing the oral short-consent process and this English consent form has been approved by the IRB for use as the basis of translation.

Witness:

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.

PRINCIPAL INVESTIGATOR: Raffit Hassan, M.D.

STUDY TITLE: A Phase I Study of the Mesothelin-Targeted Immunotoxin LMB-100 with or without *Nab*-Paclitaxel (Abraxane) in Patients with Malignant Mesothelioma

STUDY SITE: NIH Clinical Center

Cohort: Part B -LMB-100 combination therapy

Consent Version: 03/01/2020

WHO DO YOU CONTACT ABOUT THIS STUDY?

Raffit Hassan, M.D. by phone at 240-760-6232 or email raffit.hassan@nih.gov

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

If the individual being asked to participate in this research study is not able to give consent to be in this study, you are being asked to give permission for this person as their decision-maker. The term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research, throughout the remainder of this document.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

In this study, we will determine a safe dose of LMB-100 in patients with advanced mesothelioma with or without *nab*-paclitaxel. LMB-100 is an investigational agent, meaning that it has not been approved by the US Food and Drug Administration. It is a type of manufactured protein which is similar to protein normally produced by your body in response to a specific foreign substance. LMB-100 is attracted to the mesothelin protein, which is present in a lot of different tumors,

including mesothelioma, but is found in only a very small number of normal tissues. After binding to the mesothelin on tumors, LMB-100 can then attack and kill cancer cells. *Nab*-paclitaxel is an FDA approved agent used in the treatment of breast cancer, non-small cell lung cancer and pancreatic cancer. Its use in this study is investigational as it has not been approved in the treatment of mesothelioma. Part A of the study included two groups of patients (Arms A1 and A2) who were assigned to receive LMB-100 alone. In part B, two other groups (Arms B1 and B2) will be assigned to receive LMB-100 with *nab*-paclitaxel. You will participate in either Arm B1 or B2 depending on when you enroll in the study.

WHY ARE YOU BEING ASKED TO TAKE PART IN THIS STUDY?

You are being asked to take part in this study because you have pleural or peritoneal mesothelioma that has not responded to prior platinum based therapy.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 34 participants will be enrolled in the study, the first 10 in part A and the remainder in Part B.

DESCRIPTION OF RESEARCH STUDY

In Part A of the study a safe dose of LMB-100 alone has been established; however, 9 of 10 subjects who were evaluated had their tumors remain stable, while 1 subject's tumor grew. Therefore, we will enroll Part B to determine a safe dose of LMB-100 in combination with *nab*-paclitaxel.

The first 6 participants will be enrolled in the phase 1 portion of part B (Arm B1) at a slightly lower dose of LMB-100 than the safe dose of part A in combination with a *nab*-paclitaxel. If it is found to be safe, 10 additional participants will be enrolled (Arm B2) so that we may begin to determine whether the study therapy can shrink tumors. If there are too many intolerable side effects, we will test a lower dose of LMB-100 in combination with *nab*-paclitaxel in the next 6 participants and the enroll an additional 10 patients at that dose level.

You will receive LMB-100 through an IV catheter (a tube inserted in a vein, usually in your arm) on day 1, day 3 and day 5 of each 21-day cycle. You will receive LMB-100 for up to 2 cycles or until your disease worsens or you have intolerable side effects, whichever happens first. You will receive *nab*-paclitaxel through an IV on day 1 and day 8 of each 21-day cycle for up to 6 cycles or until your disease worsens or you have intolerable side effects caused, whichever happens first. We will continue to follow you after you have finished taking the study drug to keep track of your disease status (progression), your survival status or whether you have taken any additional cancer therapy. The specific procedures you will have are described below.

WHAT WILL HAPPEN IF YOU TAKE PART IN THIS RESEARCH STUDY?

Before you begin the study

Before beginning the study, you will need to undergo tests and/or procedures to help your doctor verify whether you can participate. This is called screening. Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, there are some extra procedures that you will need to have if you take part in this study. If you have already

undergone some of these examinations very recently, your doctor may decide not to repeat them. Briefly, these tests, which are performed under a separate consent, include:

- Confirmation of diagnosis (You must provide a sample tumor tissue for an evaluation by the NCI Laboratory of Pathology. The tissue may be from a previous surgery, biopsy or collection from a tumor effusion (fluid around the tumor). If none is available, we will ask you to have a biopsy or a collection of effusion material to provide a fresh sample). Please see page 10, Tumor Biopsies and Effusions for a description of the procedure.
- Medical history and physical examination
- Routine blood and urine tests including pregnancy test in women who can have children. Pregnant women will not be allowed on study.
- Scans and x-rays
- Electrocardiogram (ECG)
- Echocardiogram
- Tests for viruses (hepatitis and HIV)

During the study

Once it is determined that you are eligible and you have signed the consent for the study, you will receive IV infusions of LMB-100 and *nab*-paclitaxel. as described above. Each infusion will last about 30 minutes, but it might take longer if your study doctor decides it is needed for your safety. Each nab-paclitaxel infusion also lasts about 30 minutes. On day 1 of each cycle, when both medications are given, you will receive the LMB-100 about 30 minutes after you have completed the nab-paclitaxel infusion. You will be monitored for side effects for 2 hours after the first infusion, and for 30 minutes after all other infusions if no side effects occurred previously. We will give you standard pre-medications that include an antihistamine (such a Benadryl), acetaminophen (Tylenol), ranitidine (Zantac) and dexamethasone, a steroid to help prevent infusion related side effects.

While you are taking study medication, we will perform a number of tests and examinations for safety and to test the effect of the study therapy.

These include routine blood and urine tests that will be done 4 – 5 times per cycle, a chest X-ray on day 1 of each cycle, scans that will be performed approximately every 6 weeks, and ECGs that will be done just before each infusion.

We will also perform tests for research studies to find out how your body handles the drug (PKs), the types of immune cells present in your disease, how your body reacts to the drug and how certain side effects of the LMB-100 might be caused. Most of the sampling for these research tests will be done before your first dose of study drug, on the days you take the study drug (just before or just after you get the study drug) or at the end of treatment. In addition, a blood sample will be collected at the end of cycle 2 and on day 8 of the first two cycles. Exceptions to this are:

- PK studies will be performed on days 1 and 5 of cycles 1 and 2. Except for the cycle 2 day 5 sample, which will only be drawn immediately before and after the LMB-100 infusion, these samples will be drawn before your infusion and periodically for up to 6 hours after the start of infusion.

- Optional biopsies which may be collected before the first dose of LMB-100 (if you have not given a biopsy at screening) and after you have completed two cycles of therapy. The biopsies to be performed are exclusively for research purposes and will not benefit you. It might help other people in the future. You will be given the opportunity to decide whether you want to have these sample collected at the time of each biopsy. All tissue will be reviewed by the NCI Laboratory of Pathology.

When you are finished taking the drugs

Approximately 4 – 6 weeks after you have had your last dose of study drug, you will be asked to return to the NIH for a follow up visit to have the following tests:

- Medical history and physical exam
- Routine blood and urine tests
- Scans if your disease has not worsened since the beginning of the study
- ECG

If after this visit, your disease remains stable or improves, you will continue to be scanned every 6 weeks until your disease worsens.

About once a year, regardless of whether your disease has gotten worse, we will contact you or your physician by telephone to ask about any other cancer therapies you may have started and about your survival status.

BIRTH CONTROL

If you are a woman who is breast feeding or pregnant, you may not take part in the study because we don't know how this medicine would affect your baby or your unborn child. If you are a woman who can become pregnant, you will need to practice an effective form of birth control before starting study treatment, during study treatment, and for 3 months after you finish study therapy. If you become pregnant while receiving study medication or within 28 days after taking your last dose of study medication, you must tell the study doctor right away. If this happens, study medication will be discontinued. The study doctor will follow you and your pregnancy to completion.

If you are the male partner of a woman who can become pregnant you will need to practice an effective form of birth control in addition to using a condom and refrain from donating sperm before starting study treatment, during study treatment, and for 6 months after you finish study therapy. You should also refrain from sperm donation during this time period. If your partner becomes pregnant while you are receiving study medication or within 6 months after you took your last dose of study medication, you must tell the study doctor right away.

Effective forms of birth control include:

- abstinence from heterosexual contact
- intrauterine device (IUD)
- hormonal [birth control pills, injections, or implants]
- tubal ligation

- vasectomy

RISKS OR DISCOMFORTS OF PARTICIPATION

Risks and Possible Undesirable Effects of LMB-100

Prior to this study LMB-100 has only been given to 15 subjects; therefore, we do not know all of the possible side effects. However, below is a list of the most common and most serious side effects occurring on the earlier study, some occurring at higher doses than will be used in this study.

The most common side effects (some were serious) were:

- Low levels of the blood protein albumin which may lead to swelling, muscle weakness or loss of appetite
- Tiredness
- Swelling of the arms and legs
- Nausea
- Fever
- Decreased appetite
- Shortness of breath
- Pain in muscles

Less common, but serious side effects included:

- Fluid in the organs which may cause low blood pressure, shortness of breath, swelling of ankles
- Abnormal heartbeat
- Reactions during or following the infusion of the drug which may cause fever, chills, rash or low blood pressure
- Pain in joints
- Kidney damage which may cause swelling, may require dialysis

Other possible side effects

Other possible side effects discussed below are based on side effects that occurred when testing a similar agent, SS1P and in animal studies of LMB-100. It is possible that there may be other unexpected side-effects that occur in addition to those listed below.

LMB-100 may cause inflammation to membranes causing chest pain, shortness of breath, low blood pressure, and heart failure. In animals, some mild kidney toxicity was seen, characterized by increased enzymes and protein in the urine. This will be checked for with regular blood and urine tests.

As with other drugs similar to LMB-100, there is a chance that the drug could cause the body to produce an unwanted response called 'Anti-drug antibodies' (ADAs). These might not cause problems however there is a chance they could lead to a severe anti-drug response in the body. ADA levels will be measured during the study to monitor any changes.

There may also be pain and swelling at the infusion site.

It is important that you contact your doctor as soon as you experience any side effects whether you think the treatment has caused them or not. You must also tell your doctor if you have started any new medication or had a change to your existing medication. This includes medications available without a prescription (over the counter) and alternative medicines. If you have any questions or concerns about any of the information provided above, about the possible side effects of treatment, or the possible consequences of treatment for those side effects, please ask the principal investigator or the research staff for more information.

The most important symptoms you need to report to your doctor <u>immediately</u> are:

- possible infusion or allergic reactions (symptoms that start during or within a few hours of the infusion, e.g., wheezing, tightness in the throat or chest, rash, and facial swelling)
- chest pain
- shortness of breath
- palpitations (fast heart beat)
- bleeding and high fever
- impaired brain function (e.g., dizziness, blurred vision, confusion)

If you experience any severe or dangerous side effect, you should:

1. Seek professional medical help immediately.
2. Call your study doctor.
3. If necessary, go to the nearest emergency room.

Risks of *nab*-paclitaxel

VERY COMMON, SOME MAY BE SERIOUS In 100 people receiving nab-paclitaxel, more than 9 and up to 100 may have:	
• anemia (a decrease in the number of red blood cells which may make you feel weak or tired) • low number of white blood cells with or without fever (that may make it easier get infections) • a decrease in the number platelets, the cells that help your blood to clot (which may lead to unusual bleeding or bruising under the skin) • constipation • diarrhea • nausea • vomiting	• pain (including muscle, joints, bone, and chest pain) • swelling caused by fluid held in the tissues, especially of the ankles, feet or fingers • fever • chills • decreased appetite • change in taste • weight loss • difficulty sleeping • depression • cough • shortness of breath

VERY COMMON, SOME MAY BE SERIOUS In 100 people receiving nab-paclitaxel, more than 9 and up to 100 may have:	
• stomach pain • pain, swelling or sores on the inside of the mouth • neuropathy, a disorder of the nerves which can cause tingling or numbness, with weakness, or decreased sensation or movement • dizziness • headache • feeling tired or weak	• hair loss • rash, possibly red, bumpy or generalized • itchiness • changes in nails, including discoloration or separation from nailbed • abnormal liver function test results • dehydration (loss of water and minerals in the body) • nose bleed • decreased potassium levels in the blood

COMMON, SOME MAY BE SERIOUS In 100 people receiving nab-paclitaxel, from 1 to 9 may have:	
• a severe reduction of red or white blood cells and platelets (at nearly the same time) which can cause weakness, bruising, or make infections more likely • infections, including pneumonia or of the lung, mouth, gallbladder, urinary tract, nail, or hair follicle • a very severe infection of the blood which may include a decrease in blood pressure • inflammation of the lung passages • thickening, inflammation or scarring in the lungs which may cause breathlessness, cough • inflammation of the bowel causing abdominal pain or diarrhea • blockage of the intestine • trouble swallowing • indigestion or upset stomach • abnormal chemistry or electrolyte blood test results • abnormal kidney function test results	• nasal congestion • mouth or throat pain • dry mouth, nose, and throat • coughing up blood or bloody sputum • blood clot in the lungs or in deep vein • fluid in the chest cavity • red or flushed skin • dry skin • hand-foot syndrome, involving reddening, swelling, numbness and peeling of palms and soles of feet • high blood pressure • low blood pressure • a decrease in the heart's ability to pump blood to all parts of the body and possibly heart failure • faster heart beat • watery eyes • changes in vision or blurry vision • infusion site reactions (described as discomfort, bleeding or bruising/swelling at the needle site, and

COMMON, SOME MAY BE SERIOUS In 100 people receiving nab-paclitaxel, from 1 to 9 may have:	
• acute kidney failure • blood in the urine • lack of muscle coordination • muscle weakness • anxiety	in some instances infection or leaking of IV fluid outside of blood vessel into the surrounding tissue) • localized swelling due to buildup of lymph fluid

UNCOMMON, SOME MAY BE SERIOUS In 100 people receiving nab-paclitaxel, fewer than 1 may have:
• irregular or slow heart beat • stopping of the heart • allergic reaction (may include skin inflammation, rash, trouble breathing, trouble speaking, fever), sometimes fatal • syndrome involving abnormal blood clotting, with decreased platelets, bruising (including tiny red or purple spots under the skin) and possibly leading to blood clots • edema/swelling and cyst formation of the macular area of the retina • irritation and redness of the thin membrane covering the eye • inflammation of the cornea • too much fluid in the body • feeling unwell • sleepiness • scaly or peeling skin • potentially life threatening allergic reaction of the skin and oral mucous membranes (may include lesions in the mouth, itching and blistering skin) • hives • a loss of nerve function in the muscles of the face

Additional side effects observed during post-marketing surveillance of *nab*-paclitaxel, not otherwise noted above include:

- lack of movement in the vocal cords with possible voice changes
- skin sensitivity to sunlight
- potentially life threatening allergic reaction [may include skin rash with skin blistering]
- skin or tissue damage from prior radiation therapy can become damaged again, when a person receives chemotherapy after having had radiation therapy. This is referred to
- as radiation recall and may involve redness, peeling, pain, and swelling. Skin changes have been noted to range from mild redness to tissue death. Radiation recall

- may also occur in the lungs and other internal organs.

Elderly

In subjects ≥ 65 years old with metastatic breast cancer who received *nab*-paclitaxel monotherapy, a higher incidence of nose bleed, diarrhea, dehydration (loss of water and minerals in the body), feeling tired or weak and swelling caused by fluid held in the tissues, especially of the ankles, feet or fingers has been reported.

Birth Defects

Nab-paclitaxel may cause serious birth defects. Please refer to the section about birth control for more information on how to protect yourself if you are a female who is able to get pregnant or a male patient who has a partner who is able to get pregnant. *Nab*-paclitaxel can cause irreversible infertility in male patients. Male patients should seek advice on conservation of sperm prior to treatment.

Risks from pre-medications

Acetaminophen

Acetaminophen is considered to be safe and effective in the recommended doses. However, when taken incorrectly acetaminophen can cause liver damage. Your risk of liver damage may be increased if you drink more than three alcoholic drinks every day, take more than the recommended dose (overdose), or if you take any additional drugs that also contain acetaminophen at the same time.

Diphenhydramine

Drowsiness, dizziness, constipation, stomach upset, blurred vision, or dry mouth/nose/throat may occur when taking diphenhydramine.

Ranitidine:

It can cause constipation, diarrhea, headache, nausea or upset stomach. Rare serious side effects include severe allergic reaction with rash, hives, itching, difficulty breathing; confusion, dark urine, depression, fast or slow heartbeat, unusual bruising or bleeding, yellowing of the eyes or skin (indicating liver damage).

Dexamethasone:

Stomach upset, headache, dizziness, changes in your period, trouble sleeping, increased appetite, or weight gain may occur. Rarely patients using dexamethasone have experienced increased infection, bone/joint pain, thirst, increased urination, irregular heartbeat, eye pain, vision problems, black stools, vomit that looks like coffee grounds, puffy face, swelling of the feet and ankles, pain/redness/swelling of the arms or legs, tiredness, mood changes, unusual hair/skin growth, muscle cramps, weakness, easy bruising/bleeding, slow wound healing, thinning skin and seizures.

Risks from Study Procedures

The following study procedures and treatments may have risks and cause discomfort while you participate on this study:

Blood draws

There is the risk of slight pain, bruising or infection when your blood is drawn. Drawing blood may cause some people to faint.

ECGs

The glue used to keep the electrodes in place during the ECG may irritate your skin and cause redness.

Tumor Biopsies and Effusions

Tumor biopsies and tumor effusions: local anesthesia of the skin will be given prior to any tumor biopsy or effusion collection, in order to prevent painful sensations. However, you may still experience pain or discomfort at the biopsy site. Irritation, redness, swelling and/or bleeding may also occur. There is a risk of abnormal healing, fever, infection or of an allergic reaction to the anesthetic agent used to anesthetize the skin at the biopsy site. Once the sample has been obtained, a stitch may be used to close the wound and facilitate healing.

In some cases, we may use CT scans to help guide us during your biopsy. This introduces the added risk of research radiation. This research study may involve exposure to radiation from up to 2 CT guided tumor biopsies**.** This radiation exposure is not required for your medical care and is for research purposes only. The amount of radiation you will receive in this study is 1.5 rem which is below the guideline of 5 rem per year allowed for research subjects by the NIH Radiation Safety Committee. The average person in the United States receives a radiation exposure of 0.3 rem per year from natural sources, such as the sun, outer space, and the earth's air and soil. If you would like more information about radiation, please ask the investigator for a copy of the pamphlet, An Introduction to Radiation for NIH Research Subjects.

While there is no direct evidence that the amount of exposure received from participating in this study is harmful, there is indirect evidence it may not be completely safe. There may be a very slight increase in the risk of cancer.

Please tell your doctor if you have had any radiation exposure in the past year, either from other research studies or from medical tests or care, so we can make sure that you will not receive too much radiation. Radiation exposure includes x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body.

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

The aim of this study is to find a safe dose for this experimental treatment. We do not know if you will receive personal, medical benefit from taking part in this study. These potential benefits could include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer. Because there is not much information about the drug's effect on your cancer, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?

Instead of being in this study, you have these options**:**

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Please talk to your doctor about these and other options.

STOPPING THERAPY

Your doctor may decide to stop your therapy for the following reasons:

- if he/she believes that it is in your best interest
- if your disease comes back during treatment
- if you become pregnant
- if you have side effects from the treatment that your doctor thinks are too severe
- if new information shows that another treatment would be better for you

In this case, you will be informed of the reason therapy is being stopped.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to collaborators or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases can**not** be recalled and destroyed.

CONFLICT OF INTEREST

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a Protocol Review Guide. You may ask your research team for a copy of the Protocol Review Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines but they do not need to report their personal finances to the NIH.

Members of the research team working on this study may have up to $15,000 of stock in the companies that make products used in this study. This is allowed under federal rules and is not a conflict of interest.

The National Institutes of Health and the research team for this study have developed a drug being used in this study. This means it is possible that the results of this study could lead to payments

to NIH scientists and to the NIH. By law, government scientists are required to receive such payments for their inventions. You will not receive any money from the development of LMB-100.

Celgene is providing nab-paclitaxel for this study to NIH without charge. No NIH investigator involved in this study receives payments or other benefits from any company whose drug, product or device is being tested. However, there are some non-NIH collaborators on this study who may receive payments or benefits, limited by the rules of their workplace.

USE OF SPECIMENS AND DATA FOR FUTURE RESEARCH

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that it may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. The amount and form

of these payments are determined by the NCI Travel and Lodging Reimbursement Policy. You will be given a summary of the policy which provides more information.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- If some tests and procedures are performed outside the NIH Clinical Center, you may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- Qualified representatives from Celgene, the pharmaceutical company who produces nab-paclitaxel

When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Raffit Hassan, M.D., raffit.hassan@nih.gov, 240-760-6232. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR	Print Name of LAR	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only: This section is only required if you are doing the oral short-consent process and this English consent form has been approved by the IRB for use as the basis of translation.

Witness:

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.