Informed Consent/Authorization for Participation in Research

Title of Research Study: Phase 1 Dose Escalation and Dose Expansion Trial of NP-101 in Patients with Solid Tumors

Study Number: 2024-0500

Principal Investigator: Aung Naing, MD

_____ _____
Participant's Name Medical Record Number

Key Information

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

Why am I being invited to take part in a research study?

You are invited to take part in a research study because you have a type of solid tumor.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

The goal of this clinical research study is to learn about the safety and tolerability of the study drug NP-101 in patients with solid tumors.

This is an investigational study. NP-101 is not FDA approved or commercially available. It is currently being used for research purposes only.

The study doctor can explain how the study drug is designed to work.

How long will the research last and what will I need to do?

You may continue taking NP-101 for as long as the doctor thinks it is in your best interest. You will no longer be able to take the study drug if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

You will be asked to visit the study clinic about 1 time every 4 weeks while taking NP-101 to have tests and procedures, such as physical exams, blood collection, and imaging scans. When you stop taking the study drug, you will have a follow-up visit at about 30 days after your last dose, and then you will be followed every 12 weeks after that to check on how you are doing.

More detailed information about the study procedures can be found under ***"What happens if I agree to be in this research?"***

Is there any way being in this study could be bad for me?

Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment.

If you take part in this study, you may have mild gastrointestinal side effects, such as nausea, vomiting, constipation, and abdominal pain and/or swelling.

More detailed information about the risks of this study can be found under ***"Is there any way being in this study could be bad for me? (Detailed Risks)"***

Will being in this study help me in any way?

The study drug may help to control the disease. Future patients may benefit from what is learned. However, it cannot be promised that there will be any benefits to you or others from your taking part in this research.

What happens if I do not want to be in this research?

Participation in research is completely voluntary. You can decide to participate, not participate, or stop participation at any time without penalty or loss of your regular benefits.

Instead of taking part in this study, you may choose to receive standard treatment of the type of solid tumor you have. You may choose to receive other investigational therapy, if

available. These alternative treatments have risks and benefits that may be the same or different than those in this research study. The study doctor can discuss these alternative treatments, including their possible risks and benefits, with you.

You may choose not to have treatment for cancer at all. If you decide that you don't want any more active treatment, one of your options is called "comfort care." Comfort care includes pain medication and other support. It aims to maintain your comfort and dignity rather than cure disease. Usually, this care can be provided at home. If you think you might prefer comfort care, please discuss this with your family, friends, and your doctor.

In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

Detailed Information

The following is more detailed information about this study in addition to the information listed above.

Who can I talk to if I have questions or concerns?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at 713-563-1930.

This research has been reviewed and approved by the MD Anderson Institutional Review Board (IRB – an ethics committee that reviews research studies). You may talk to them at 713-792-6477 or IRB_Help@mdanderson.org if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

How many people will be in this study?

It is expected about 35 people at MD Anderson will be enrolled in this research study.

What happens if I agree to be in this research?

Screening Tests
Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will help the doctor decide if you are eligible:

- You will have a physical exam.

- You will have an EKG and either an echocardiogram (ECHO) or MUGA scan to check your heart function.
- Blood (about 3 teaspoons) and urine will be collected for routine tests.
- You will have a CT or MRI scan to check the status of the disease.
- You will have a tumor biopsy for biomarker testing. Biomarkers are found in the blood/tissue and may be related to you reaction to the study drug. The study doctor will tell you what type of biopsy you will have and its risks.
- If you can become pregnant, blood (about 1 teaspoon) will be drawn for a pregnancy test. To take part in this study, you must not be pregnant.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other options will be discussed with you.

Study Groups

If you are found to be eligible to take part in this study, you will be assigned to a study group based on when you join this study. Up to 15 participants will be enrolled in Part 1, and up to 20 will be enrolled in Part 2.

If you are enrolled in Part 1, the dose of NP-101 you receive will depend on when you join this study. The first group of participants will receive the starting dose level of NP-101. If no intolerable side effects are seen, the next group will receive a higher dose level of NP-101. If intolerable side effects are seen, the next group will receive a lower dose level of NP-101. One (1) of these 3 doses will be chosen as the highest tolerable dose of NP-101.

In Part 2, the highest tolerable dose of NP-10 that was found in Part 1 and possibly a lower dose will be given to learn more about the safety and effects of NP-101. Up to 10 participants will be enrolled per dose level. If you are enrolled in Part 2, you will receive 1 of the 2 doses based on when you join the study.

If you are enrolled in Part 1, you may be rolled over to Part 2 when it opens. This will be discussed with you.

The study doctor will tell you what study group you are assigned to and the dose of NP-101 you will receive.

Study Drug Administration

You will take NP-101 capsules by mouth 2 times a day, every day of each 28-day cycle. Each dose should be taken about 12 hours apart (for example, 1 morning dose and 1 evening dose) and at about the same time each day.

NP-101 should be taken with a full glass (about 1 cup) of water and may be taken with or without food. NP-101 may cause digestive symptoms (such as nausea, hiccups, or

abdominal pain), so taking NP-101 with food may help relieve these symptoms. In this case, NP-101 should be taken at about 1 hour after a meal.

If you miss a dose of NP-101, wait and take the next dose as scheduled. If you vomit a dose, do not take another dose. Wait and take the next dose as scheduled.

You will be given a medication diary to write down when you take each dose of study drug and if you miss or vomit a dose. Bring this medication diary and any unused study drug capsules (or the empty bottles) with you to each study visit.

On Day 1 of each cycle, you will wait to take your morning dose until you are at the study clinic and the study staff tells you to take it. The study staff will remind you of this.

Study Visits

On **Day 1 of each cycle**:

- You will have a physical exam.
- Blood (about 5 teaspoons) will be drawn for routine tests and pharmacokinetic (PK) testing. PK testing measures the amount of study drug in the body at different time points. At Cycle 1, blood will also be used for biomarker testing.
- You will have a CT or MRI scan to check the status of the disease.
- If you can become pregnant, blood (about 1 teaspoon) or urine will be collected for a pregnancy test.

On **Day 28 of Cycles 2 and beyond or before the dose on Day 1 of the next cycle**, blood (about 2 teaspoons) will be drawn for biomarker testing.

Every 2 cycles for 6 months and then every 3 cycles after that, you will have a CT or MRI scan to check the status of the disease.

End-of-Dosing Visit

As soon as possible after your last dose of study drug:

- You will have a physical exam.
- Blood (about 3 teaspoons) will be drawn for routine tests.

Safety Follow-Up Visit

About 30 days after your last dose of study drug or before you start a new anticancer therapy, whichever comes first:

- You will have a physical exam.
- Blood (about 3 teaspoons) will be drawn for routine tests.

Follow-Up

If you stop taking the study drug for any reason other than the disease getting worse, you will have a CT or MRI scan every 12 weeks to check the status of the disease. This

will continue until you withdraw from the study, you start a new anticancer therapy, the disease gets worse, or the study ends.

If the disease gets worse or you start a new anticancer therapy, the study staff will call you every 12 weeks to check on how you are doing. Each call will last about 10 minutes. This will continue until you withdraw from the study or the study ends. If the study staff is unable to contact you, they may review medical records, public records, or other public platforms to collect this information.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for the following:

- Tell the study team about any symptoms or side effects you have, follow study directions, and come to all study appointments (or contact the study team to reschedule).
- Tell the study doctor/study staff about all medications that you are taking or plan to take, including prescription and over-the-counter medications, supplements, vitamins, and herbal remedies.

What happens if I say yes, but I change my mind later?

You can leave the research at any time; it will not be held against you. You may withdraw from participation in this study without any penalty or loss of benefits. If you withdraw from this study, you can still choose to be treated at MD Anderson.

If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor who can help you safely stop study treatment. It may be dangerous to suddenly stop study treatment. The study doctor will also decide if you need to have any visits or tests to check on your health.

If you stop being in the research, already collected data may not be removed from the study database. You may be asked whether the study doctor can collect data from your routine medical care. If you agree, this data will be handled the same as research data.

Is there any way being in this study could be bad for me? (Detailed Risks)

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Side effects will vary from person to person, and some may occur after you have stopped receiving treatment. Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs/procedures.

NP-101 Side Effects

Based on studies of NP-101 in humans, NP-101 may cause the following side effects:

• nausea • vomiting • weight loss	• abdominal pain and/or swelling • constipation	• liver damage • kidney failure • hiccups

Other Risks

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

Having **biopsies** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the collection. An allergic reaction to the anesthetic may occur. A scar may form at the collection site.

EKGs and ECHOs may cause discomfort while lying on the exam table, and the tape on the EKG pads may cause skin irritation.

MUGA scans may cause allergic reactions to the radioactive tracer, injection site soreness, and/or swelling. They may cause damage to cells or tissue from being exposed to the radiation used in the scan. These side effects may occur in less than 10% of patients.

During an **MRI**, you may feel mild vibrations throughout your body. The machine will produce a loud knocking noise. This is normal. You will be given earplugs to protect your ears. Some people, especially those who tend to feel uncomfortable in small or closed spaces, may feel “closed in” and become anxious while in the scanner. The scanner has an intercom, which will allow you to speak to the staff during the procedure. If you feel ill or anxious during scanning, tell the MRI staff and the scanning will be stopped if you wish.

The magnetic field used in MRI scanning may harm you if you have certain types of metal in your body (as might be found in pacemakers, neurostimulators, or certain clips). It may cause problems with devices, such as pacemakers. If you have metal in your body or devices such as a pacemaker, you should discuss this with the study doctor.

If an MRI contrast material is used, your study doctor will tell you about possible side effects or allergic reaction. Contrast agents can cause allergic reactions and kidney damage. Allergic reactions can include mild itching associated with hives but can also result in a serious life-threatening emergency from difficulty breathing. If this occurs, it is treatable. The MRI will require a catheter to be inserted into one of your veins in order to inject the MRI contrast agent. This may cause skin irritation, bleeding, and/or infection.

CT scans send x-rays through the body at many different angles. You will be exposed to a small dose of radiation. All radiation adds up over a lifetime and may increase the risk of new cancer forming. Some people may feel “closed in” while lying in the scanner. However, the scanner is open at both ends, and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or radiology technicians will give comfort, or the scanning will be stopped. Solution may also be given by vein to make the x-ray pictures more accurate. This may cause an uncomfortable feeling of warmth, nausea, and/or severe allergic reactions. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching.

Although every effort will be made to keep study data safe, there is a chance that your personal health information could be lost or stolen, which may result in a **loss of confidentiality**. All study data will be stored in password-protected computers and/or locked file cabinets and will continue to be stored securely after the study.

In addition to these risks, this research may hurt you in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death.

You will be told about any new information that may affect your health, welfare, or choice to stay in the research.

Pregnancy Related Risks
Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant, breastfeed a baby, or father a child while on this study.

Birth Control Requirements: If you can become pregnant or father a child and you are sexually active, you must use birth control during the study and for at least 60 days after your last dose of study drug. Talk to the study doctor about the method(s) of birth control you should use.

If you can become pregnant, acceptable methods of birth control include:

- Combined (estrogen- and progestogen-containing) hormone birth control pills, vaginal rings, or patches that stop ovulation (the release of eggs)
- Progestogen-only hormonal birth control pills, implants, or injections that stop ovulation
- Intrauterine device (IUD) or intrauterine hormone-releasing system (IUS)
- Bilateral tubal occlusion (“tubes tied”)

- Vasectomized partner (with the absence of sperm confirmed) as your only male sexual partner

If you are a male, you must use a condom. You should tell your sexual partner(s) about your participation in this study, and your partner should also consider using one of the birth control methods listed above.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant will result in your removal from this study.

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy.

Will it cost anything to be in this study? Will I be paid to be in this study?

NP-101 will be provided at no cost to you during this study.

You and/or your insurance provider will not have to pay for certain research exams and procedures done that are covered by the study.

You and/or your insurance provider will be responsible for the costs of routine clinical services (such as diagnostic/therapeutic procedures, drugs, devices, laboratory assays, and other services that would ordinarily be ordered for medical care, regardless of whether or not you are participating in a study). There may be extra costs that are not covered by your medical plan that you will have to pay yourself.

Taking part in this study may result in added costs to you (such as transportation, parking, meals, or unpaid leave from work). You may have to pay for medication prescribed to treat or prevent side effects, and you may have to visit the clinic/hospital more often than if you were not participating in this study.

If you have insurance, talk to your insurance provider and make sure that you understand what your insurance pays for and what it does not pay for if you take part in this study. Also, find out if you need approval from your plan before you can take part in the study.

You may ask that a financial counselor be made available to you to talk about the costs of this study.

You will not receive any compensation for taking part in this study.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who need to review this information. Complete secrecy cannot be promised. Organizations that may inspect and copy your information include the IRB and other representatives of this organization.

A participant study number will be assigned to you once you have been enrolled in the study. This participant study number will be used to identify your data in the study report and when reporting any data from the study.

Any personal information that could identify you will be removed or changed before data are shared with other researchers or results are made public.

The sponsor, monitors, auditors, the IRB, and the Food and Drug Administration will be granted direct access to your medical records to conduct and oversee the research. By signing this document, you are authorizing this access.

Federal law provides additional protections of your medical records and related health information. These are described below.

Will my data or samples be used for future research?

Your personal information and/or samples are being collected as part of this study. These data and/or samples may be used by researchers at MD Anderson or shared with other researchers and/or institutions for use in future research.

In some cases, all of your identifying information may not be removed before your data or research samples are used for future research. If future research is performed at MD Anderson, the researchers must get approval from the MD Anderson IRB before your data and/or research samples can be used. At that time, the IRB will decide whether or not further permission from you is required. If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

If identifiers are removed from your identifiable private information or identifiable samples that are collected during this research, that information or those samples could be used for future research studies or shared with another researcher for future research studies without your additional informed consent.

Some of your specimens and genetic and/or health information might also be placed into one or more external publicly accessible scientific databases. Your name and other information that could directly identify you (such as your address or social security number) will never be placed into these external databases. A researcher who wants to study information from these databases must have an approved study and work with the group overseeing the database to obtain the information.

Can I be removed from the research study without my permission?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include if the disease gets worse, if intolerable side effects occur, if you are unable to follow study directions, or if the study is stopped.

What happens if I get hurt from being in this study?

If you get sick or hurt and it is related to your participation in this study, you will be given care at MD Anderson (if you are at the clinic when you are sick or hurt). If you get hurt or sick and you are not at the clinic (for example, you are at home or at another doctor's office):

- call your personal doctor right away (or in an emergency, call 911)
- tell your personal doctor or ER staff that you are in this study (try to give them a copy of this consent form or show them your participant card)
- call the study doctor (Dr. Aung Naing, at 713-563-1930) or 713-792-2121 (24 hours)

You will not be reimbursed for expenses or compensated financially by MD Anderson for this injury. Costs of treatment received because you were hurt or sick will be billed to you or your insurance company. No other form of payment is available.

You may also contact the MD Anderson IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

What else do I need to know?

This research is being supported by Novatek Pharmaceuticals.

MD Anderson may benefit from your participation and/or what is learned in this study.

Your information and samples (both identifiable and de-identified) may be used to create products or to deliver services, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family.

This research study involves genetic testing, which will include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you.

The Genetic Information Nondiscrimination Act (GINA) prohibits health insurers or health plan administrators from requesting or requiring genetic information of you or your family members, or using such information for decisions regarding your eligibility for insurance or your premiums. However, this law does not provide the same protection for disability, life insurance, or long-term care insurance. GINA also prohibits most employers (with 15 employees or more) from using genetic information when making decisions on your employment, including decisions related to hiring, firing, promotion, pay, and job assignments. Please contact the study doctor if you would like more information about GINA and how it protects you from genetic discrimination.

Optional Procedures for the Study

You do not have to agree to the optional procedures in order to take part in this study. There are no benefits to you for taking part in the optional procedures. Future patients may benefit from what is learned. You may stop taking part at any time. There will be no cost to you for taking part in the optional procedures.

Optional Procedure #1: If you agree, you will have a biopsy on Day 28 of Cycle 2 for biomarker testing. The study doctor will tell you what type of biopsy you will have.

Optional Procedure #2: Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health and if you agree, the researchers will contact you to let you know what they have found.

If the researchers return genetic test results to you, it may be because they think you could have a health risk and want to recommend that the test should be re-done by a certified clinical laboratory to check the results. If this happens, then you may want to get a second test from a certified clinical laboratory, consult your own doctor, or get professional genetic counseling. You may have to pay for those additional services yourself.

Optional Procedure Risks:

Having biopsies performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the collection. An allergic reaction to the anesthetic may occur. A scar may form at the collection site.

Receiving research results that have meaning for your health may cause distress.

CONSENT/PERMISSION/AUTHORIZATION FOR OPTIONAL PROCEDURES
Circle your choice of "yes" or "no" for each of the following optional procedures:

Optional Procedure #1: Do you agree to have a biopsy on Day 28 of Cycle 2 for biomarker testing?

YES NO

Optional Procedure #2: Do you agree that the researchers can contact you if the research with your identifiable information or samples gives results that have meaning for your health?

YES NO

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:
   - Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
   - The IRB and officials of MD Anderson
   - Novatek Pharmaceuticals, who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study, and/or licensees of the study technology
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

   Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

   The results of this research may be published in scientific journals or presented at medical meetings. However, your identity will not be disclosed. Your name and other identifying information will be kept confidential.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will do its best to protect the privacy of your records, but it is possible that once information is shared with people listed on this form, it may be released to others. If this happens, your information may no longer be protected by federal law.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

E. 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.

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under this protocol.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for non-English speakers utilizing the short form consent process (VTPS) and patients who are illiterate.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line.)