Site Name

Protocol Title:	A Phase II Trial of Poly-ICLC for Progressive, Previously Treated Low-Grade Gliomas in Children and Young Adults with Neurofibromatosis Type 1
IND Number:	43984
IRB Protocol #:	IRB-300005076
Sponsor:	Department of Defense, U.S. Army
Sponsor Protocol #:	NF111
Support from:	Oncovir, Inc.
Principal Investigator:	Site PI

For Children (persons under 18 years of age) participating in this study, the term "You" addresses both the participant ("you") and the parent or legally authorized representative ("your child").

General Information	You are being asked to take part in a research study. This research study is voluntary, meaning you do not have to take part in it. The procedures, risks, and benefits are fully described further in the consent form.
Purpose	The purpose of the study is to find out if a tumor fighting drug called Poly-ICLC will work on decreasing the size of low-grade gliomas in pediatric patients with Neurofibromatosis Type 1 (NF1).
Duration & Visits	You will receive drug for up to 2 years of treatment and up to 5 additional years for follow up. You will come to clinic once a month for up to 28 visits the first two years. Then you will come to clinic every 3-12 months for follow-up for approximately 10 visits over the 5 additional years. You will be involved in the study for up to 7 years. Each visit should last between 1-3 hours.
Overview of Procedures	Over the course of the study, you will get Poly-ICLC intramuscular injections twice a week for 24 cycles. Each cycle is approximately 28 days. The dose of Poly-ICLC will be calculated by your weight. Every 4 weeks, you will be evaluated in clinic or any reactions to Poly-ICLC. Every 12 weeks you will have an MRI to see if your tumor is shrinking. If your tumor is on the optic pathway you will have eye exams every 12 weeks. If the tumor is growing, you will be taken off the study.
Risks	The most common risks include muscle soreness and redness where the drug is injected. A complete listing of the risks is included in the "Risks and Discomforts" section later in this form.
Benefits	The potential benefit is to stop the growth and/or decrease the symptoms you feel from your progressive low-grade glioma. It is possible that you

	will not respond to the treatment. The study doctors hope to be able to use the information to determine the effectiveness of this medication on this tumor type. We also hope that information learned from this study will help other patients with NF1 and low-grade gliomas in the future.
Alternatives	Other possible alternatives are surgery, treatment with other experimental therapies or commercially available drugs, or receive no antitumor therapy and only receive treatment for your symptoms.

Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. You may also decide to discuss this study and this form with your family, friends, or doctor. If you have any questions about the study or about this form, please ask us. If you decide to take part in this study, you must sign this form. We will give you a copy of this form signed by you for you to keep.

Purpose of the Research Study

This is a clinical trial, a type of research study. Your study doctor, Site PI, and his associates from the Site Name will explain the clinical trial to you.

We are asking you to take part in a research study because you have been diagnosed with Neurofibromatosis Type 1 (NF1) and have progressive low-grade gliomas.

The purpose of this research study is to test how well a new drug called Poly-ICLC works in treating children with NF1 and progressive low-grade gliomas. The new drug, Poly-ICLC, is investigational and not yet approved by the Food and Drug Administration (FDA). Poly-ICLC has been used in children and adults with different types of brain tumors in other research studies like this one. Earlier studies showed that this drug worked better for children and young adults with low-grade gliomas than for children with more aggressive brain tumors.

In this study, investigators will use Poly-ICLC treatment in a larger number of patients with NF1 and previously treated low-grade gliomas to see how well it works and how many side effects occur in these patients. This is a Phase II study. A Phase II study is a research study that tests the effectiveness of the drug and monitors side effects of a drug.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 20 participants will take part in this study at multiple sites across the United States, and about XXX people will participate at Site Name.

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

Study Participation & Procedures

Your participation in this research study will involve up to 28 scheduled visits for 2 years while you are receiving drug, with an additional 28 visits for follow-up that will last an additional 5 years. You will be part of this study for up to 7 years. To monitor if there has been a response to treatment, you will have an MRI (Magnetic Resonance Imaging test) and an eye exam (if your tumor is on the pathway that affects your vision) every 12 weeks. Your participation in this research study will last until the study drug stops working and your tumors grow. Each of these visits will take between 1 – 5 hours, depending on what tests are needed.

You are not allowed to take certain medications during the research study. Before taking medications other than the study drug (such as a prescribed drugs, over-the-counter drugs like allergy medications, cough and cold remedies, pain relievers, vitamins, herbs and minerals), you must first ask the study doctor. If you need to have surgery while on this study, please contact the study doctor.

If you agree to participate in this research study and you sign this informed consent form, you will be asked to participate in screening tests and procedures (described below) to determine if you are eligible for participation in this study.

Before you begin the main part of the study...

Screening/Baseline Study Visit (will last about 4 - 5 hours)

The following tests and procedures will be performed:

- You will have a physical examination, neurological exam and your vital signs will be measured (pulse, blood pressure, oxygen saturation, breathing rate and temperature)
- You will be asked about your medical history and about any medications you have taken in the past or are currently taken.
- The study doctor will check your performance status to monitor your ability to function and perform activities of daily living.
- About 1-2 teaspoon (5-10ml) of blood will be drawn from a vein in your arm for laboratory testing including testing to see how well your bone marrow, kidneys and liver are working.
- If you are a female who is able to have children, you will have a pregnancy test (either with some of the blood drawn or with urine). If the results of this pregnancy test are positive, you will not be able to participate in this study.

- An eye exam with an Ophthalmologist (doctor that specializes in eye and vision care) for patients with optic nerve tumors.
- You will have an MRI of your brain and spine to find out the location and size of tumors. An MRI is a body scanning technique that uses magnetic waves to look at organs and soft tissues in the body. This will be done to identify the tumors before starting therapy. You will be asked to lie down on the MRI table. The table will move into a long chamber inside the MRI machine. The space is open at both ends. You will hear loud tapping or knocking for which you may wear earplugs. An MRI lasts about 45 minutes to 1 hour and you will need to lie still for the entire time. A small amount of contrast agent is usually injected into your vein before an MRI. The contrast agent helps make the pictures clear.

  You will have a spine MRI only if your tumor is in the spine or your doctor feels this is necessary based on your symptoms.
- You and/or your parent/guardian will be asked to complete a questionnaire about how your disease affects your activities in daily life.

During the main part of the study...

If the results of these screening tests and procedures show you can participate in this study, you will be asked to return to the study clinic for the study drug portion of this study. All study participants will get Poly-ICLC.

Several required tests such as the MRI and eye exam (for patients with optic nerve tumors) may not be scheduled on the same day for a study visit due to your availability and/or available appointments. This could require you to come in up to 3 separate days.

Study Treatment with Poly-ICLC:

- You will get injections of Poly-ICLC into muscle two times weekly. The first treatment will be given in the clinic so nurses and doctors can make sure you do not have any (allergic) reaction to the injection. They will also teach you or a caregiver how to safely give the injections. If you tolerate the injections and do not have a severe reaction, then the rest of the injections will be given at home.

- The medicine will be supplied in vials and you will be taught how to pull the medicine out of the vials safely. You will also be given syringes that have a line on the syringe showing the amount of medicine to put into the syringe. The vials should be kept in the refrigerator, but not frozen. They can be left at room temperature for up to 3 days without losing effectiveness.

- If you forget to administer the medication, you need to contact your physician to get instructions of when to give the medication again, but no closer than 48 hours between doses.

- While you are receiving Poly-ICLC, you will be asked to keep a temperature log, noting your temperature before you receive the Poly-ICLC, and again at 12 hours after you get the drug for the first 28 days or cycle one. After the first 28 days, your temperature will be monitored if needed. Temperature may be taken orally, under the arm, skin or in the ear. Your doctor will review the log with you. You will need to bring this log with you each time you come to the clinic.

- You will also be asked to keep a medication diary, noting the date, time, place of the injection and any problems you had when taking the Poly-ICLC. This will be done with every dose of Poly-ICLC and you will need to bring this diary with you each time you come to the clinic.

- While you are on this study, information about how you are doing will also be collected. This will include what medications you are taking, any side effects from the treatment that happen and the status of your disease.

  Recommended days to receive Poly-ICLC injections:

	Option 1*	Option 2*
Monday	**X**	
Tuesday		**X**
Wednesday		
Thursday	**X**	
Friday		**X**
Saturday		
Sunday		

*If you miss a dose of medication on the scheduled day, a dose can be given up to 24 hours later. Injections must be separated by at least 48 hours.

Day 1 (will last about 2 hours):

- You will have a physical examination, neurological exam and your vital signs will be measured.
- You will be asked about any medications you have taken or are currently taking.
- The study doctor will check your performance status to monitor your ability to function and perform activities of daily living.

- About 1-2 teaspoons (5-10 ml) of blood will be drawn from a vein in your arm for a baseline to compare to future tests to see how well the drug is working.
- If you are a female who is able to have children, you will have a pregnancy test (either with some of the blood drawn or with urine).
- You will get your first injection of Poly-ICLC into your muscle. The nurses and doctors will make sure you do not have any (allergic) reaction to the injection. They will also teach you or a caregiver how to safely give the injections. If you tolerate the injections and do not have a severe reaction, then the rest of the injections will be given at home.

Day 8 (will last about 0.5 hour)

- About ½ -2 teaspoon (2-10ml) of blood will be drawn from a vein in your arm for laboratory testing including testing to see how well your bone marrow is working.
- An additional 1-3 teaspoons (5-15ml) of blood will be collected at the same time the 2-10ml is collected (as described above). This will not require another needle prick. This blood will be tested to look at how well the drug works, as part of this study.

Day 15 (will last about 1 hour):

- You will have a physical examination, neurological exam and your vital signs will be measured.
- You will be asked about your medical history and about any medications you have taken in the past or are currently taken.
- Review of any side effects you may be experiencing.
- Review of drug/temperature diary.
- The study doctor will check your performance status to monitor your ability to function and perform activities of daily living.
- About ½ -2 teaspoon (2-10ml) of blood will be drawn from a vein in your arm for laboratory testing including testing to see how well your bone marrow is working.
- An additional 1-3 teaspoons (5-15ml) of blood will be collected at the same time the 2-10ml is collected (as described above). This will not require another needle prick. This blood will be tested to look at how well the drug works, as part of this study.

Study Visits for Beginning of Cycles 2-24 and Off-Study (will last about 1 - 4 hours depending on when you have your MRI and ophthalmology exam):

The following tests and procedures will be performed every 28 days (once every 4 weeks):

- You will have a physical examination, neurological exam and your vital signs will be measured.
- You will be asked about any medications you have taken or are currently taking.
- Review of any side effects you may be experiencing.
- Review of drug/temperature diary.
- The study doctor will check your performance status to monitor your ability to function and perform activities of daily living.
- About 1-2 teaspoon (5-10ml) of blood will be drawn from a vein in your arm for laboratory testing including testing to see how well your bone marrow, kidneys and liver are working.
- If you are a female who is able to have children, you will have a pregnancy test (either with some of the blood drawn or with urine). If the results of this pregnancy test are positive, you will not be able to continue participating in this study, and your participation will end.
- At the beginning of cycles 3, 6 and 12 and 30 days after receiving the last dose of drug, an additional 1-3 teaspoons (5-15 ml) of blood will be collected at the same time the 5-10 ml is collected (as described above). This will not require another needle prick. This blood will be tested to look at how well the drug works, as part of this study.
- You and/or your parent/guardian will be asked to complete a questionnaire about how your disease affects your activities in daily life at the end of Cycle 6 and 12 and after 30 days receiving the last dose of drug.
- In addition to your monthly physical and laboratory examinations, you will have an MRI to see whether your tumors are responding to therapy and an eye exam with an Ophthalmologist (for patients with optic pathway gliomas) beginning of Cycles 4, 7, 10, 13, 16, 19, 22, and 30 days after receiving the last dose of drug.

The study doctor will discuss with you your responsibilities as a participant.

After you have stopped the study drug……

You will have the off treatment follow up visit about 30 days from the last dose of the study drug for a physical exam, vital signs, blood test and to make sure you don't have any residual side effects from the study drug if you come off treatment due to side effects or progression.

After all the study drug is stopped, you will have periodic physical exams as part of your regular care to see if the tumors are growing or have come back. We would like to learn about how patients are doing after stopping the study drug.

Study Visits for the first 12 months after you have stopped taking drug – Year 3 of study (will last about 1.5 - 3 hours depending on when you have your MRI and ophthalmology exam):

The following tests and procedures will be performed:

- At the end of the 3rd month and 12 month, an additional 1-3 teaspoons (5-15 ml) of blood will be collected. This blood will be tested to look at how well the drug works, as part of this study.
- Every 3 months, you will have an MRI to see whether your tumors are responding to therapy and an eye exam with an Ophthalmologist (for patients with optic pathway gliomas).

Study Visits for the 13 to 36 months after you have stopped taking drug – Year 4 and 5 of study (will last about 1.5 - 3 hours depending on when you have your MRI and ophthalmology exam):

The following tests and procedures will be performed:

- After the 24th month after you have stopped taking drug, you and/or your parent/guardian will be asked to complete a questionnaire about how your disease affects your activities in daily life.
- Every 6 months, you will have an MRI to see whether your tumors are responding to therapy and an eye exam with an Ophthalmologist (for patients with optic pathway gliomas).

Study Visits for the 37 – 60 months after you have stopped taking drug – Year 6 and 7 of study (will last about 1 - 2 hours depending on when you have your MRI and ophthalmology exam):

The following tests and procedures will be performed every 12 months:

- You will have an MRI to see whether your tumors are responding to therapy and an eye exam with an Ophthalmologist (for patients with optic pathway gliomas).

Study Visit if you have PROGRESSION between 1 to 60 months after you have stopped taking drug – Year 3 through Year 7 of study (will last about 45 minutes):

- You will have 1-3 teaspoons (5-15 ml) of blood collected. This blood will be tested to help understand how the drug worked, as part of this study.
- You and/or your parent/guardian will be asked to complete a questionnaire about how your disease affects your activities in daily life if you have tumor progression before 24 months post-therapy.

Risks and Discomforts

You may have some side effects from taking the study drug. All medications have side effects. Poly-ICLC has been used safely in children and adults at this dose and at higher doses in other research studies. Frequently seen side effects include irritation of the skin where the injection is made and mild flu-like symptoms. These are usually relieved or avoided by use of over-the-counter medicines like acetaminophen (Tylenol) or ibuprofen (Advil, Motrin).

Side Effects of Poly-ICLC Include:

	Common (21-100 patients per 100)	**Occasional (5 to 20 patients per 100)**	**Rare (1 to 4 patients per 100)**
Immediate (within 1 to 2 days of receiving the drug)	Muscle soreness and redness where the drug is injected.	Diarrhea	
Prompt (within 2 to 3 weeks)		Fatigue Muscle aches Joint aches Fever Chills	Decreased number of white blood cells
Delayed (anytime later during therapy)			Increased liver enzymes levels in the blood

Many side effects go away shortly after the medications are stopped, but in some cases side effects can be serious, long lasting or permanent. Your doctor will be checking closely to see if any of these side effects are occurring. Routine physical examinations, eye exams and blood tests will be performed once a month or more frequently to look for side effects of the drug.

Tell the study team right away if you have any new or worsening symptoms, so that the cause can be determined and adequate treatment can be provided. All problems need to be reported to the study doctors or study nurses looking after you either by phone or at the next visit.

Some drugs or supplements may interact with your treatment plan. Talk to your doctor, pharmacist, or study team before starting any new prescription or over-the-counter drugs, herbals, or supplements and before making a significant change in your diet. Supplements may come in many forms, such as teas, drinks, juices, liquids, drops, capsules, pills, or dried herbs. All forms should be avoided.
For more information about risks and side effects, you should feel free to ask your study doctor. If you are concerned about your health between visits due to participating in this trial, please call the emergency telephone numbers provided.

There may be additional side effects related to Poly-ICLC that your treating team still does not know. It is very important to tell them if you have any bad experiences while on this study.

Other risks:

Blood Draw Risks: Risks associate with needle sticks for drawing blood are slight, but some possible risks include excessive bleeding, fainting or feeling lightheaded, bruising, infection (a slight risk any time the skin is broken), and multiple punctures to locate veins.

Quality of Life Questionnaire: Some of the questions in the interview are about anxiety and depression and may make you feel uncomfortable. You do not have to answer any questions you do not want to answer. All answers you do give will be kept private. Although your answers are private, there is a slight chance that your information might be seen by someone who is not supposed to see it.

MRI Risks: Because the MRI machine acts like a large magnet, it could move iron-containing objects in the MRI room during your examination, which in the process could possibly harm you. Precautions have been taken to prevent such an event from happening; loose metal objects, like pocketknives or key chains, are not allowed in the MRI room. If you have a piece of metal in your body, such as a fragment in your eye, aneurysm clips, ear implants, spinal nerve stimulators, or a pacemaker, you will not be allowed into the MRI room and cannot have an MRI.

Having an MRI may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia and by the loud banging noise during the study. Temporary hearing loss has been reported from this loud noise. This is why you will be asked to wear earplugs. At times during the test, you may be asked to not swallow for a while, which can be uncomfortable.

Because the risks to a fetus from MRI are unknown, pregnant women must not participate in this study.

Contrast agent (gadolinium) risks: A few side effects of gadolinium injection such as mild headache, nausea, and local pain may occur. Rarely (less than 1% of the time) low blood pressure and lightheadedness occurs. This can be treated immediately with intravenous fluids. Very rarely (less than one in one thousand), participants are allergic to gadolinium. These effects are most commonly hives and itchy eyes, but more severe reactions have been seen which result in shortness of breath.

Participants with severe kidney disease sometimes have a bad reaction to gadolinium contrast. The condition is called nephrogenic systemic fibrosis (NSF). It can cause skin to tighten or scar and can damage internal organs. Sometimes it can be life-threatening. There are no reports of NSF in participants with normal kidney function. Before you have an MRI scan requiring an injection of gadolinium contrast, you will have a blood test in order to check the function of your kidneys. Based on your medical history and the results of the test, a doctor will decide whether it is safe for you to undergo the MRI scans.

Confidentiality risks: There is a risk someone could get access to the personal information in your medical records or other information researchers have kept about you. Someone might be able to trace this information back to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information. In some cases, this information could be used to make it harder for you to get or keep a job. There are laws against misuse of genetic information, but they may not give full protection. The researcher believes the chance these things will happen is very small but cannot promise that they will not occur.

Sedation Risks:
If you need sedation for any procedure, you will get a separate consent form that explains the risks of sedation.

Information for Women of Childbearing Potential, Nursing Mothers, and/or Men Capable of Fathering a Child

Patients who are pregnant or breast-feeding cannot take part in this study. Poly-ICLC may hurt an embryo, fetus or nursing child. Women capable of becoming pregnant must have a negative pregnancy test before entering the study. For females who are able to become pregnant and sexually active, you must practice an effective method of birth control during the treatment and for 3 months after stopping the treatment.

Recommended methods of birth control are:

- the consistent use of an approved oral contraceptive (birth control pill)
- an intrauterine device (IUD)
- hormone implants (Norplant)

- contraceptive injection (Depo-Provera)
- double barrier methods (diaphragm with spermicidal gel or condoms with contraceptive foam)
- sexual abstinence (no sexual intercourse)
- sterilization

Oral contraceptives, hormone implants, and injections are only considered effective if used properly and started at least one month before beginning the study, continuing throughout the study, and for 3 months after the study.

A pregnancy test will be given to females of childbearing potential before therapy begins. **Because the drug in this study can affect an unborn baby, you should not become pregnant or father a baby while on this study. You should not nurse a baby while on this study. If a female caregiver is pregnant or suspects she is pregnant, she should not handle Poly-ICLC.** If you become pregnant during the study, you will need to inform your doctor immediately and stop taking Poly-ICLC. The principal investigator may ask you to provide information about the outcome of your pregnancy and the health of your baby. Ask about counseling and more information about preventing pregnancy.

Note to Men
Because the effects of participating in this study on sperm are unknown, male patients, whose sexual partner(s) are women of childbearing potential, are required to use adequate contraception during the study and for 3 months after the end of treatment, using one of the methods described above. If your partner becomes or thinks she may have become pregnant during the time you are in the study or within one month after stopping the study drug, you must tell the principal investigator right away. The principal investigator may ask for your partner's permission to collect information about the outcome of her pregnancy and the health of her baby. The principal investigator will discuss with you whether you have to stop taking part in the study if your partner becomes pregnant for safety reasons.

What Will Be Done to Minimize the Risks?
The doctor and/or staff will be checking you closely to see if any of the side effects are occurring. Most side effects go away after the treatment is stopped. The doctor may prescribe drugs to lessen or control side effects. Treatment will be modified, whenever necessary, to prevent permanent damage. The doctor will do everything possible to prevent any serious complications. If they do occur, your doctor will provide appropriate measures (blood transfusions, antibiotics, anti-vomiting medications, etc.).

Although you will be treated according to a specific plan (protocol), individual circumstances may arise. In such cases, your health will always be considered more important than strictly following the protocol. Changes will be discussed before they are made whenever possible.

Benefits

It is hoped that the use of Poly-ICLC will control your disease, but this cannot be guaranteed. We also hope that information learned from this study will help improve treatment for other patients who have NF1 progressive low-grade gliomas in the future. There may be no direct benefit from participating in this study.

Alternatives

You may decide not to take part in this research study without any penalty. The choice is totally up to you. You do not have to participate in this study to receive ongoing care for your condition. The study doctor will discuss with you the alternatives to participation and their risks and benefits.

Alternatives to this therapy include:

- use of drugs or other therapies that have been previously tried in the treatment of this disease
- surgery
- no anti-tumor therapy at this time
- palliative care, which treats the symptoms and quality of life, rather than the disease.

PLEASE TALK TO YOUR DOCTOR AS WELL AS OTHER TRUSTED PROFESSIONALS AND FAMILY ABOUT THESE AND ANY OTHER OPTIONS.

Confidentiality and Authorization to Use and Disclose Information for Research Purposes

Insert site HIPAA language

A Data and Safety Monitoring Board (DSMB), the National Cancer Institute, a research monitor, Department of Defense, Oncovir Inc., members of the Neurofibromatosis Consortium and a site monitor will be reviewing the data from this research throughout the study.

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

Voluntary Participation and Withdrawal

If you decide to take part in the study, you may withdraw from participation at any time without penalty or loss of benefits to which you would otherwise be entitled. However, if you are thinking of leaving the study, we ask that you speak with a study team member about this decision. Leaving this study early will not affect your regular medical care.

If you do decide to withdraw your consent, we ask that you contact Site PI and let him know that you are withdrawing from the study. The mailing address is Site Mailing Address. If you wish to withdraw

your Authorization as well as your consent to be in the study, you must contact the study doctor in writing.

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped, or your participation ended at any time by your physician, or the study sponsor, without your consent because:

- The principal investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The study sponsor, the principal investigator, the Food and Drug Administration (FDA) or other body responsible for monitoring the safety of the study has decided to stop the study.

Cost of Participation

Oncovir, Inc., the makers of Poly-ICLC, is supplying the drug at no cost to you, and providing support to conduct this study.

Taking part in this study may lead to added costs to you or your insurance company. You or your insurance company will be charged for all of the costs associated with your standard clinical care, such as the laboratory tests, MRIs, eye exams, and clinic visits described in this consent form. These are considered part of standard care for someone with your illness. However, you will not be responsible for the cost of the study drug. Oncovir, Inc. will provide the Poly-ICLC free of charge to participating research participants.

Your individual insurance or government health insurance program may not cover certain services, items or procedures. You may want to discuss this with your insurance carrier in advance. You will be responsible for any co-payments and/or deductibles for standard clinical care services rendered. If you believe you have received a bill for a research related procedure contact the study team at Site Telephone Number or the billing office that sent the bill.

The costs of your standard medical care will be billed to you and/or your insurance company in the usual manner.

If you have any questions, your doctor and the study team will be able to provide you with answers. For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call **1-800-4-CANCER (1-800-422-6237)** and ask them to send you a free copy.

Payment for Participation in Research:

You will not be paid for taking part in this study.

Treatment and Compensation for Injury:

Insert Site Injury Language

The Department of Defense, Oncovir Inc., and the Neurofibromatosis Consortium have made no provision for monetary compensation in the event of injury from the research, and in the event of such injury, treatment will be provided, but is not free of charge.

WHAT ARE MY RIGHTS IF I TAKE PART IN THIS STUDY?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you, and you will not lose any of your regular benefits.

Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

You are not waiving any of your legal rights by signing this consent form.

WHO CAN ANSWER MY QUESTIONS ABOUT THIS STUDY?

You can talk to your study doctor about any questions, concerns, or complaints about the research, or a research-related injury, including available treatments. Contact your study doctor, Site PI or his/her associates at Site Telephone Number.

Site IRB/HRPP contact information

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855-860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday.

Significant New Findings

During the course of this study we may find more information that could be important to you. This includes information that might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available. The investigator will tell you about new information from this or other studies that may affect your health, welfare, or willingness to stay in this study.

Optional Consent

Consent for Use of Study Data for Future Research:

If you agree, we would like to keep your data containing personal information such as your medical history, eye exam and imaging results, and adverse events for future research about NF, treatments for these conditions, and ways to prevent these conditions.

The data will be labeled with a unique study identification number, instead of your name. The data will be used for research purposes only and will not benefit you. It is also possible that the stored data may never be used. Results of research done on your data will not be available to you or your doctor. Your data will be stored indefinitely. We may give this data about you to other researchers or companies not at Site Name. The results might help people who have NF in the future.

Your information may be put in controlled-access databases. This means only researchers who apply for and get permission to use the information for a specific research project will be able to access the information. Your information stored in these databases will not include any identifying information. We will replace identifying information with a code number. We will keep a master list that links your code number to your identifying information at Site Name. Only certain study personnel for this study at Site Name will have access to this master list. Researchers approved to access information in the controlled-access database will agree not to attempt to identify you.

Consent for Use of Leftover Blood for Future Research:

Donating your blood for future research is completely voluntary.

You will have blood collected as part of your participation in this clinical trial at baseline, day 8 and day 15 of cycle 1, day 1 cycles 3, 6 and 12, at the end of therapy or at the time of progression during treatment, 3 months post treatment, 1-year post treatment, and at time of progression when off treatment if applicable. After the study has been completed, instead of discarding your leftover specimens, with your permission, we will save (bank) them for possible future research to learn more about cancer and other diseases. Any leftover blood samples will be coded and stored indefinitely at the Dhodapkar Laboratory at Emory University in Atlanta, Georgia.

The research that may be done with your blood specimens are not designed specifically to help you. It might help people who have NF and other diseases in the future.

Reports about research done with your blood will not be given to you or your doctor. These reports will not be put in your health record. The research will not have an effect on your care. If the research is published or presented at scientific meetings, your name and other personal information will not be used.

Consent to Collect Tumor Tissue and blood sample:

You might have had surgery to determine the type of tumor you have before beginning this study. As part of this study, we would like to use any left-over tissue from that surgery for this study. The tissue will be banked at the Children's Hospital of Philadelphia for possible future research.

If you have tumor surgery while on this study, we would like your permission to use any left-over tissue from that surgery as well. Surgeries will not be done solely for the study. This is a request to use any left-over tissue that has been stored by the hospital that was not used for evaluation of your disease. We would also like to collect 10 mL (2 teaspoons) of blood.

Things to Think About

If you decide now that your study data and/or left over blood and/or tumor tissue with blood samples can be used for future research, you can change your mind at any time. Just contact the study doctor, Site PI, at Site Name at Site Address and let us know that you do not want us to use your blood or study data.

Then any samples that remain or stored study data that has not already been shared will no longer be used for research. We will destroy any remaining identifiable specimens and information if they are no longer needed for your care. However, if any research has already been done using portions of your specimens or study data, the data will be kept and analyzed as part of those research studies.

Your blood and study data will be used only for research and will not be sold. The research done with your blood specimen and study data may help to develop new products in the future. You will not receive any payment or financial benefit from any products, tests, or discoveries derived from these samples.

Confidentiality risks: There is a risk someone could get access to the personal information in your medical records or other information researchers have kept about you. Someone might be able to trace this information back to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information. In some cases, this information could be used to make it harder for you to get or keep a job. There are laws against misuse of genetic information, but they may not give full protection. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

Research use of your private information and biospecimens will be conducted in compliance with applicable regulatory requirements.

Risks associated with genetic testing:

If you agree to allow blood to be banked for future research, the research studies on your samples may involve genetic analyses, and these data may be shared with other researchers. The risks related to

genetic analyses can be to individuals or to groups. These harms include stigmatization and insurability. To reduce this risk, only coded samples will be stored and used for research. Information about this study will not be recorded in your medical record.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and some employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

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

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance, nor does it protect you against genetic discrimination by all employers.

Making Your Choice

Please think about your choice. After reading, **put your initials** next to the "Yes" or "No" statement. If you have any questions, please talk to your doctor or nurse.

If the subject/parent does not speak English, the person obtaining consent should initial the subject's/parent's choice below.

The choice to let us use your **study data** for future research is optional and is up to you. No matter what you decide to do, it will not affect your care.

_____ Yes, I will allow my **study data** to be kept for use in future research about NF and other diseases.

_____ No, I will NOT allow my **study data** to be kept for use in future research about NF and other diseases.

The choice to let us keep any **leftover blood** for future research is optional and is up to you. No matter what you decide to do, it will not affect your care.

_____ Yes, I will allow my **leftover blood** to be kept for use in future research about NF and other diseases.

_____ No, I will NOT allow my **leftover blood** to be kept for use in future research about NF and other diseases.

The choice to let us collect any **tumor sample and blood sample** for future research is optional and is up to you. No matter what you decide to do, it will not affect your care.

_____ Yes, I agree to allow for **tumor tissue and blood sample** (from pre-study surgery and surgeries during study) to be used for use in future research about NF and other diseases.

_____No, I do NOT agree to allow for **tumor tissue and blood sample** (from pre-study surgery and surgeries during study) to be used for use in future research about NF and other diseases.

DOCUMENT OF CONSENT:

PARTICIPATION IN RESEARCH IS VOLUNTARY.

You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.
My signature below indicates that I agree to participate in this study. I am aware that I will receive a copy of this signed agreement:

- I have had enough time to read the consent or have the consent form read to me and think about participating in this study;
- I am willing to participate in this study;
- I have been told that my participation is voluntary, and I can withdraw at any time

PARTICIPANT NAME: _____
(Print Name)

_____ _____
Date Participant's Signature for Consent

_____ _____
Date Signature of Participant 14 Years of Age and Older

_____ _____
Date Signature of Parent or Guardian

_____
Name of Legally Authorized Representative (if applicable) / Relationship of Legally Authorized Representative to Participant

_____ _____
Date Signature of Legally Authorized Representative (if applicable)

_____ _____
Date Witness Signature
(Only required if the participant is a non-English speaker)

Waiver of Assent

The assent of _____ (name of child/minor) was waived because of:

Age _____

To be completed by person obtaining consent:

For Adult Participants:

☐ The participant is an adult and provided consent to participate.

☐ The participant is an adult who lacks capacity to provide consent and his/her legally authorized representative:

- ☐ gave permission for the adult participant to participate
- ☐ did not give permission for the adult participant to participate

For Minor Participant:

☐ The parent or legally authorized representative gave permission for the minor to participate.

☐ Parent or legally authorized representative is illiterate.

The consent form was read to the parent or legally authorized representative who was given the opportunity to ask questions.

☐ The parent or legally authorized representative did not give permission for the minor to Participate.

Signature of Individual obtaining consent: _____

Printed name of above:_____

Date: _____