NF110: Open-label, Phase 2 Clinical Trial of Crizotinib for Children and Adults with Neurofibromatosis Type 2 and Progressive Vestibular Schwannomas

Informed Consent

NCT04283669

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Site Name

Protocol Title:	Open-label, Phase 2 Clinical Trial of Crizotinib for Children and Adults with Neurofibromatosis Type 2 and Progressive Vestibular Schwannomas
IND Number:	EXEMPT
IRB Protocol #:	IRB-300003645
Sponsor:	Department of Defense, U.S. Army
Sponsor Protocol #:	NF110
Support from:	Pfizer, 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 the maximum tumor shrinkage in participants that have NF2 and vestibular schwannomas using a drug called crizotinib.
Duration & Visits	You will be in this study for up to 14 months with an option to continue if you are eligible. You will come to the clinic once a month during that time for a total of 14 visits. Each visit should last between 1 and 5 hours, depending on what tests are needed.
Overview of Procedures	Over the course of the study, you will take crizotinib twice a day if you are 18 years or older. If you are less than 18 years old, the amount will be determined by your age, height, and weight. Every four weeks, you will be evaluated in the clinic for any reactions to crizotinib. Every 12 weeks you will have an MRI and a hearing exam to see if the tumor is shrinking. If the tumor is growing, you will be taken off the study.
Risks	The most likely risks are vision problems, constipation, nausea, diarrhea, vomiting, swelling of the body, tiredness, loss of appetite, and liver damage. Additional important risks are further described in the Risks and Discomforts section of this document.
Benefits	There may be no benefit from participating in this study. A potential benefit could be to slow the growth and spread of your disease, but you may not respond to treatment.
Alternatives	Other possible alternatives are surgery, treatment with another experimental therapy or commercially available drugs, or receive no anti-tumor 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, Dr. SITE PI, and his/her associates from the SITE will explain the clinical trial to you.

You are being asked to join this study because you have been diagnosed with Neurofibromatosis Type 2 (NF2) and have growing NF2-related tumors (abnormal growths of body tissue) called vestibular schwannomas (VS) or progressive hearing loss.

The purpose of this study is to determine if the study drug, crizotinib, has any effect on tumors found in patients with NF2. NF2 is a condition that mainly affects the skin and nervous system. It causes non-cancerous tumors to grow on the nerves around a person's body. Some signs of NF2 include a gradual loss of hearing and tumors growing on the skin, the brain, and the spinal cord, which can lead to complications.

Crizotinib is an oral drug (taken by mouth) that is approved by the United States Food and Drug Administration (FDA) for the treatment of other types of tumors. However, in this research study, crizotinib is considered investigational because it is not approved by the FDA for treatment of your medical condition (NF2). We know a lot about how well it is tolerated (handled), but we do not know if it is effective in treating your condition. This research study will test whether crizotinib may shrink tumors commonly found in patients with NF2 or stop them from growing. This will help us to decide if Crizotinib should be used to treat NF2 patients in the future.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 19 people will take part in this study at multiple sites across the United States, and about ## people will participate at SITE.

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

Study Participation and Procedures

Your participation in this research study will involve 14 scheduled visits during the first year, with the possibility of extending treatment further if you benefit from it. To monitor if there has been a response to treatment, an MRI (Magnetic Resonance Imaging test) and audiogram (hearing test) (for patients with remaining hearing) will occur 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 and 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, including measurement of your vital signs (pulse, blood pressure, breathing rate, and temperature), height, and weight.
- You will be asked about your medical history and about any medications you have taken in the past or are currently taking.
- You will have an electrocardiogram (ECG), a test that allows the electrical activity of your heart to be studied. This is done to make sure you do not have any pre-existing heart disease. You will be asked to lie down and sticky pads will be attached to each arm, leg, and the chest while the electrical activity of the heart is recorded. You will be asked to remain still for 10-15 minutes.
- You will have a detailed eye exam performed by an ophthalmologist, a doctor that specializes in eye and vision care.
- The study doctor will check your performance status to monitor your ability to function and perform activities of daily living.
- You will have an MRI of your brain 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 be asked to have an audiogram (hearing test) to look at your hearing loss if you have measurable hearing.
- About 1 teaspoon (5cc) 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, some of this blood will also be used for a pregnancy test. If the results of this pregnancy test are positive, you will not be able to participate in this study.

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 crizotinib. A supply of crizotinib will be given to you at each study visit which will occur every 4 weeks. If you are 18 years of age or older you will take 250 mg of crizotinib orally twice a day, approximately 12 hours apart. If you are less than 18 years of age, the dose (amount) of crizotinib you take will be determined by your age, height, and weight. You should take crizotinib in the morning and evening, at approximately the same time every day with or without food.

We will ask you to keep a log of the pills or amount of liquid you take with a diary. We will review and collect the diary after each cycle. We define one treatment course as 28 days. We will work with you to schedule end of course visits outlined below.

If you vomit or miss a dose, an additional dose should not be taken. Just skip the missed dose and take the next dose at the usual time. You will be asked to store crizotinib tablets at room temperature. Keep the container closed tightly. Keep medicine out of the reach of children. You will be asked to return any unused study drug at each study visit.

You will be asked to report all changes in your physical condition to the study doctor and/or the study team during the study visits, even if you do not believe they are related to the study. Your study doctor will be monitoring you closely for any side effects that may be caused by this study drug and may change the dose if it is harmful.

Several required tests such as the eye test, hearing test, MRI and ECG 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.

Day 1/Prior to treatment (will last about 1 hour)

The following tests will be performed:

- You will have a physical examination, 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 1/2 teaspoons (8cc) 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, some of this blood will also be used for a pregnancy test.
- If you are 16 years old or older, you will be asked to complete one questionnaire. If you are 18 years old or older, you will be asked to complete a second questionnaire regarding tinnitus (ringing in your ears). These questionnaires will ask you about how your disease affects your life activities such as housework, studying, sports, and family life. It will take you about 5 minutes to complete each questionnaire.

This study visit may be on the same day as your screening/baseline visit. If the Day 1 study visit cannot be scheduled on the same day as your screening/baseline visit, it needs to occur within 4 weeks of the screening/baseline visit. If it is more than 4 weeks, the screening/baseline visit needs to be repeated.

If your screening visit and Day 1 visit are not on the same day, the study investigator will contact you within a week after your screening visit to let you know if you qualify for the study. At this time, your Day 1 visit will be scheduled.

Study Visits for End of Cycles 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 and Off-Study (will last about 1 - 5 hours depending on when you have your MRI and audiogram)

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

- You will have a physical examination, and your vital signs will be measured at every visit.
- You will be asked about any medications you have taken or are currently taking.
- Review of any side effects you may be experiencing.
- The study doctor will check your performance status to monitor your ability to function and perform activities of daily living.
- About 1 teaspoon (5cc) 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, some of this blood will also be used for a pregnancy test. 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 end of cycles 1, 3, and 12, an additional 1 1/2 teaspoons (8cc) of blood will be collected at the same time the 5cc 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. This test will not be repeated if you participate in the retreatment therapy.
- If you are 16 years old or older when you started the study you 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. If you are 18 years old or older when you started the study, you will be asked to complete a 2nd questionnaire regarding tinnitus (ringing in your ears).
- At the end of cycles 1, 3, 6, 9, 12, and you will have an eye exam by an ophthalmologist. In between these examinations, if at any time you develop vision changes or a new eye problem occurs, another eye exam by an ophthalmologist (eye doctor) may be necessary, and may be repeated if vision disorder persists or worsens in severity.
- In addition to your monthly physical and laboratory examinations, you will have an MRI to see whether your tumors are responding to therapy, an audiogram (hearing test) to measure your hearing, and ECG to see how your heart is working at the end of Cycles 3, 6, 9, 12, and Off-Study,

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

After you have stopped taking the study drug…
You will have the Off treatment follow-up visit 30-35 days after the last dose of study drug for physical exam, vital signs, and blood tests to make sure you don't have any residual side effects from the study drug.

After all study drug is stopped, you will have periodic MRI scans, hearing tests and physical exams as part of your regular care to see whether the tumors are growing or have come back. We would like to learn about how patients are doing after stopping the study drug. Therefore, the study team may contact your doctor and request results from these clinical tests and assessments obtained during a period of up to 18 months after you have stopped the study drug.

If your tumor starts to grow during the 24 weeks after you finish the 12 cycles of crizotinib, you will be eligible for re-treatment on the study for up to 48 additional weeks, provided you still meet study eligibility criteria. You will need all Screening/Baseline Study Visit tests and procedure repeated to see if you still qualify for the study.

Risks and Discomforts

In addition to stopping tumor cells from growing, drugs such as crizotinib can damage normal tissues. These "side effects" are called toxicities. Problems, which do arise, are usually reversible when the medication is stopped, but occasionally can persist and may cause serious complications. While on the study, there is at risk for the side effects listed below. There also may be other side effects that we cannot predict. Other drugs will be given to make side effects less serious and uncomfortable.

Risks and side effects related to crizotinib include those which are:

Most likely side effects; some may be serious (greater than 30%):

- Vision problems: Blurred vision, double vision, impaired vision, discomfort in the eyes from light, seeing spots before the eyes (floaters), flashing lights, brightness, rings, shadows, and/or streaking (63%)
- Nausea (57%)
- Diarrhea (54%)
- Vomiting (51%)
- Swelling of the body (47%)
- Constipation (43%)
- Upper respiratory infection (32%)
- Increased blood level of a liver enzyme which may mean liver damage (32%)
- Loss of appetite (30%)
- Tiredness (30%)

Less likely side effects; some may be serious (greater than 5% up to 30%):

- Dizziness (26%)
- Numbness and tingling of arms and legs (25%)
- Decrease in the total number of white blood cells which may increase chances of infection (22%)
- Changes in taste (21%)
- Slow heart rate (13%)
- Rash (13%)
- Upset stomach (8%)
- Kidney damage which may cause swelling, may require dialysis (8%)
- Increase in liver enzymes that may be a sign of damage to the liver (7%)

Side effects that occurred at a lower rate; serious (up to 4 %):

- Prolonged QT interval: a heart rhythm disorder that can potentially cause fast, unorganized heartbeats. (4%)
- Fainting (3%)
- Swelling or damage of the lungs which may cause life-threatening lung problems. Symptoms include shortness of breath, cough and fever (3%)
- Sacs of fluid in the kidneys that may cause pain (3%)
- Loss or absence of sperm (2.0%)
- Heartburn (2%)
- Liver failure (<1%)
- Severe visual loss (0.2%)

If you develop any vision symptoms such as blurriness, seeing flashes of light, light sensitivity, or floaters, double vision, impaired vision, discomfort to light, seeing spots, brightness, rings, shadows, and/or streaking, please contact your investigator right away and do not wait until the next study visit.

An increase in creatine phosphokinase (CPK) in patients was observed after crizotinib was approved by the FDA. Increased CPK can indicate stress or injury to muscle tissue. The frequency cannot be reliably estimated because this was not a standard laboratory test in the crizotinib clinical trials. We will closely watch your CPK levels when we perform other routine blood tests. We will closely watch your CPK levels when we perform other routine blood tests. If we find any symptoms related to the elevation of CPK or a significant increase in the level of CPK in your blood, you may have to temporarily stop taking the study drug, take a lower dose of the study drug for subsequent cycles, or permanently stop taking the study drug.

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 crizotinib 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: The risks of a blood draw include pain, bruising, and the slight possibility of infection at the place where the needle goes in. Some people feel dizzy or may faint during or after a blood draw.

Electrocardiogram: There is no pain or discomfort during an ECG; however, removing the pads may cause some irritation to your skin.

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.

Results from your MRI during this trial may dictate study drug treatment. There have been instances during this study where readings have led to people having unnecessary treatment. We have attempted to make changes to prevent this from happening in the future but it can still be a risk.

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 a 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 believe the chance these things will happen is very small, but cannot promise that they will not occur.

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. Crizotinib 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 crizotinib.** If you become pregnant during the study, you will need to inform your doctor immediately and stop taking crizotinib. 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 child bearing 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.
This is a new, experimental treatment for NF2-associated tumors. You may experience other, presently unknown, side effects. You will be watched closely and you will stop taking the study drug if serious side effects develop.

Benefits

There may be no direct benefit from participating in this study. The potential benefit of this treatment is to stop the growth and spread of your disease, but the response of any particular benefit can vary and you may not respond to this treatment. Whether or not this benefit occurs, the knowledge gained by this study will help optimize treatment for other patients with NF2 and tumors.

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 participation include:

- Surgery
- Treatment with another experimental therapy or commercially available drugs
- No anti-tumor therapy and only treatment of your symptoms

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

Confidentiality and Authorization to Use and Disclose Information for Research Purposes

INSTITUTION SPECIFIC LANGUAGE:
Insert your site's HIPAA and confidentiality language in this section. If your site does not have language, we will provide it.

(This is a space holder only)

A Data and Safety Monitoring Board (DSMB), the National Cancer Institute, a research monitor, Department of Defense, 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 Dr. SITE PI and let him/her know that you are withdrawing from the study. His/her mailing address is PI Address. If you wish to withdraw your Authorization as well as your consent to be in the study, you must contact Dr. PI NAME 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

Pfizer, Inc., the makers of crizotinib, 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, ECG, audiology exams, 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. Pfizer, Inc. will provide the crizotinib 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 and the SITE 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.

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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:

It is important that you tell your study doctor, SITE PI, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at PHONE NUMBER.

The SITE, Department of Defense, Pfizer 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.

INSTITUTION SPECIFIC LANGUAGE: (This is a space holder only)

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 PI PHONE NUMBER.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, contact Insert 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, audiology and imaging results, and adverse events for future research about NF2, 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, The results might help people who have NF2 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 here at SITE. Only certain study personnel for this study at SITE 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 prior to starting the study drug, and after cycles 1, 3 and 12 for analysis of biomarkers of tumor burden and response to therapy. 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 Kissil Laboratories at The Scripps Research Institute in Scripps, Florida.

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.

Things to Think About
If you decide now that your study data and/or left over blood can be used for future research, you can change your mind at any time. Just contact the study doctor, SITE PI, at the INSTITUTION, INSTITUTION ADDRESS, SITE PI's EMAIL 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 researcher 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 most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

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

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, 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 NF2 and other diseases.

_____ No, I will NOT allow my **study data** to be kept for use in future research about NF2 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.

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: _____