

SAMPLE INFORMED CONSENT

A PHASE 2a STUDY OF ULTRATRACE™ IOBENGUANE I 131 (MIBG) IN PATIENTS WITH RELAPSED/REFRACTORY HIGH-RISK NEUROBLASTOMA

A New Approaches to Neuroblastoma Therapy (NANT) treatment protocol

Molecular Insight Pharmaceuticals, Inc. (Sponsor)

INVESTIGATOR [Insert Name of Investigator]
[INSERT NAME OF INSTITUTION]
[Insert Address (include City, State and Zip Code)]
[Insert Telephone/Fax Numbers]
[Insert Email]

The word “you” used throughout this document refers to you or your child.

WHAT IS THIS STUDY ABOUT?

This study is a clinical trial, a type of research study. Clinical trials include only patients who choose to take part. Please take your time to make your decision about participating. You may discuss your decision with your friends, family, and health care team. If you have any questions, you may ask your study doctor.

You are being asked to participate in this study because you have been diagnosed with neuroblastoma, a type of solid cancer that usually affects children. Your cancer has either grown back (relapsed) or has never gone away (persistent tumor) after having received standard treatment. Standard treatment may have included chemotherapy, surgery, radiation therapy and/or high-dose chemotherapy with a stem cell transplant.

Ultratrace™ Iobenguane I 131 is an experimental agent that is not yet approved by the US Food and Drug Administration (FDA) or Health Canada. This study will be the first study to test Ultratrace™ Iobenguane I 131 in children and will help find the highest Ultratrace™ Iobenguane I 131 dose that can safely be given to patients with resistant/relapsed neuroblastoma.

WHY IS THIS STUDY BEING DONE?

The purposes of this study are:

- To find the highest dose of a new form of MIBG, Ultratrace™ Iobenguane I 131, that can be given by vein without causing severe side effects.
- To find out the side effects of Ultratrace™ Iobenguane I 131 given on this schedule at different dose levels.
- To measure how much radiation is taken up by tumors seen on a CT or MRI scan and different tissues/organs in the body after a small dose of Ultratrace™ Iobenguane I 131 is given by vein.
- To determine if your tumor gets smaller after treatment with Ultratrace™ Iobenguane I 131.
- To find out about how treatment with Ultratrace™ Iobenguane I 131 affects your quality of life at about two months after you are treated.

The research is being done because:

Currently there is no known effective treatment for your type of cancer.

MIBG is a chemical that has been used in many children to treat their neuroblastoma and is known to shrink some of the tumors, and to have tolerable side effects. MIBG is taken up by neuroblastoma tumor cells in a “lock and key” manner. Normal cells do not have the “lock” for MIBG, but neuroblastoma tumor cells do. MIBG is the key that fits into the lock. MIBG molecules can be put together with radioactive iodine (^{131}I) in the laboratory to make radioactive ^{131}I MIBG. The ^{131}I MIBG gives radiation to the neuroblastoma cancer cells and causes them to die.

This study will use a new form of MIBG called UltratraceTM Iobenguane I 131 (UltratraceTM). Ultratrace is made in a different way compared to other forms of MIBG. The Ultratrace form of MIBG has radioactive iodine attached to 20 times more MIBG molecules than the “standard” form of MIBG. This means more radioactive MIBG molecules may be given in treatment with Ultratrace and may kill more neuroblastoma cells.

Because ^{131}I -MIBG travels in the blood and gives some radiation to the bone marrow, it lowers the number of normal blood cells in the bone marrow when it is given at higher doses. It is expected that as the dose of UltratraceTM is increased, the blood cells will not recover to normal without giving back the patient’s own blood stem cells to regrow new normal blood cells. In this study, all patients will be given their own stem cells after the UltratraceTM therapy, to help regrow the normal blood cells more quickly to decrease possible side effects.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Between 15 and 24 people will take part in this study.

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

Medical Tests Before You Begin the Study

You will need to have the following exams, tests, or procedures to find out if you can be in the study. These are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- Stem Cell Collection

Before you can get treatment on this study, stem cells must be available. If you have stem cells already stored they must meet study requirements for you to be able to participate in this clinical research study.

- Physical exam
- Bone marrow tests
- Various radiology scans including CT and/or MRI and MIBG scans
- Blood tests
- Pregnancy tests for females
- Tests to check heart function (Electrocardiogram (ECG) and echocardiogram (Echo) or MUGA scan)
- Urine tests

During and at the End of the Study:

If the exams, tests and procedures show that you can be in the study, and you choose to take part, then you will need the following tests and procedures during the study. These tests will also be done at various times throughout the study and at the end of the study. The purpose of these

tests is to look for side effects of the treatment, and how to see how your neuroblastoma responds to the treatment. A table showing when these tests/procedures are done and how often they are done for the study is at the end of the consent form.

- Physical exam
- Blood tests
- Urine tests
- Various radiology scans including CT and/or MRI and MIBG scans
- ECG tests before and after imaging dose of Ultratrace™ and Holter monitor* during treatment dose of Ultratrace™

*A Holter monitor is a portable recorder you wear that records what your heart is doing. Patients wear a Holter monitor instead of having EKG tests done during Ultratrace™ treatment since the patient is in isolation because of the radiation from the Ultratrace™ treatment.

Because you are in this study, physical exams and blood tests that are part of your regular cancer care will be done more often.

EKG tests and Holter monitor that are done during the study are not part of your regular cancer care and are being done for research purposes only. The MIBG scans done 2 or 3 times (depending on if your child needs general anesthesia for the scans) are also done for research purposes and are not part of your regular cancer care.

Treatment Plan

Dosimetry (1-4 weeks before starting treatment)		Treatment		
Give Ultratrace™ imaging dose (within 7 days of study enrollment)	2-3 MIBG scans are done within 2-5 days of getting Ultratrace™ imaging dose	Day 0 Give Ultratrace™ treatment dose MIBG scan on discharge from radiation isolation	Day 14 Stem cell infusion	Day 60 End of treatment evaluation

This study is done in two parts called Dosimetry and Treatment.. Dosimetry and administration of the Ultratrace™ treatment dose will be done at the designated NANT MIBG treatment centers for this study. The stem cell infusion and end of treatment evaluation may be done at any hospital that is a part of NANT. The MIBG treatment centers are hospitals participating in NANT clinical research studies that are set up to take care of patients treated with radioactive substances. If your hospital is not one of the NANT MIBG treatment centers it means that you may need to travel some distance to another hospital to participate in dosimetry and get treatment with Ultratrace™. Your doctor will talk with you about where the different hospitals are that can perform the dosimetry and give the Ultratrace™ treatment. Your nurse and other members of the team that take care of you can help you plan the trip to get this treatment and return home for the stem cell infusion and end of treatment evaluation.

All patients/parents/legal guardians will complete a Quality of life questionnaire once before starting dosimetry and again at end of treatment with Ultratrace™ for all patients. Children 5 years and older will also answer their own questionnaire. You will answer questions about how you feel and what activities you are able to do. This will take about 10 minutes. Researchers want to see if treatment with Ultratrace™ has any effect on your quality of life.

Part One: DOSIMETRY

All patients are required to participate in dosimetry. Patients will receive one dose of Ultratrace™ over 1-3 minutes through a temporary IV catheter placed in a vein in the hand or arm or the central venous catheter. This imaging dose of Ultratrace™ is only large enough to be absorbed in the body and be seen on an MIBG scan. This dose will not treat or kill the neuroblastoma. An ECG will be done before and after the imaging dose of Ultratrace™ to determine if there are any side effects from the imaging dose on heart function. Two or three MIBG scans will be done within 5 days after getting the Ultratrace™ imaging dose. Each MIBG scan will take 30 – 45 minutes to complete. Younger children who need general anesthesia to help them lie still on the table underneath the camera will only have two MIBG scans done. From these scans researchers will look at how much radiation is absorbed from the Ultratrace™ imaging dose by different tissues of the body. They will also see if your neuroblastoma tumor absorbs the Ultratrace™. These results will be used to decide if you will go on the Part Two: Treatment.

Patients who show Ultratrace™ uptake in at least one place where there is neuroblastoma, and don't absorb more than the expected amount of radiation in normal body tissues will be treated with Ultratrace™ in part 2 of the study.

Patients whose neuroblastoma tumors do NOT take up Ultratrace™ will not be able to continue on this study and be treated with Ultratrace™. Patients whose neuroblastoma tumor does take up Ultratrace™ but has more radiation taken up by normal body tissues than researchers would expect to see will be able to continue on the study but will be treated with a lower dose of Ultratrace™ to make sure they do not have too many side effects from radiation to normal tissues.

Part Two: TREATMENT

One to four weeks after dosimetry, patients who are approved for Treatment, will begin this part of the study. Patients will be admitted to a NANT MIBG treatment center on the day before treatment. On the following day (Day 0), a treatment dose of Ultratrace™ is given over 30 to 60 minutes, through a temporary IV catheter usually placed in a vein in the hand or arm or a central venous catheter. If a temporary IV is used, it will be taken out once the Ultratrace™ infusion has finished. Fluids and other medicines that are needed will be given through the central venous catheter. A Holter monitor is a portable recorder that tracks what the heart is doing over a period of time. A holter monitor will be placed on each patient before treatment with Ultratrace™ and will be removed 24 hours later. Readings from the holter monitor will be used to determine if there are any side effects from the treatment dose on heart function.

You will be assigned a dose of Ultratrace™, which will be one of up to 4 doses studied in groups of 3-6 patients. The radiation dose given to the first group of patients treated with Ultratrace™ MIBG will be the same dose of radiation given with the lowest dose of "standard" MIBG currently used in neuroblastoma patients without bad side effects. Each group of 3 to 6 patients will receive the same dose of Ultratrace™. Once we have evaluated those patients to see what side effects have happened – then the next group of 3-6 patients will get a slightly higher dose of Ultratrace™ (called dose escalation). This process will continue until we find an unacceptable number of patients are having serious side-effects. At that point, investigators will have found the highest dose of Ultratrace™ that can be given without bad side effects. The amount of Ultratrace™ you will be given will depend on when you enter the study. Your doctor will tell you what dose you will receive and answer your questions about dose escalation. You will only receive one treatment with Ultratrace™ on this study.

Patients who are given Ultratrace™ are considered "hot" or radioactive and special precautions are taken to care for you during this time until the radiation level goes down to where these precautions are no longer needed (Usually 4 - 5 days). Special care precautions include:

- A single room in a bed surrounded by a lead shield to keep family and the staff who take care of you from being exposed to radiation from the Ultratrace™ treatment. This usually is about 5 days.
- The length of time family can visit inside the room in front of the protective lead shield that is around your bed will depend on how much radiation is measured in the room each day by the radiation specialist. Usually family can visit 30-45 minutes on the first day and longer on the days after that because there will be less radiation measured in the room each day.
- Family may visit anytime outside of the room behind a lead shield. You will be able to see who is visiting over this shield.
- No one will be able to spend the night in this special room with you during this time.

Your urine will be radioactive after treatment with Ultratrace™. A urinary catheter will be inserted through your urethra into the bladder to drain the radioactive urine from your body. This catheter will be removed 3 –5 days following the treatment.

You will also take 2 medicines by mouth, (potassium iodide and potassium perchlorate) to prevent thyroid damage from the radioactive iodine contained in the Ultratrace™. The two medicines will be taken together by mouth beginning the night before treatment for a total of 6-8 days then the potassium iodide alone will be continued for a total of 6 weeks.

Your stem cells will be given back to you intravenously by central line or by vein 14 days after being treated with Ultratrace™. The stem cells must be given at a NANT treatment center. Four hours after the stem cell infusion, patients may get granulocyte colony stimulating factor (G-CSF, a medicine to help the growth of white blood cells) given either by vein or as a shot under the skin (subcutaneous) once a day until enough white blood cells are present to fight infection. G-CSF is not required to be given, and this will be decided by your individual doctor.

HOW LONG WILL I BE ON THIS STUDY?

Patients will only receive one dose of Ultratrace™ as part of this study. You will be treated on this study until 9 weeks after receiving therapy with Ultratrace™, or for as long as it takes for your stem cells to produce enough normal blood cells. You have the option to begin other anti-cancer therapy earlier than 9 weeks after Ultratrace™ therapy if your tumor begins to grow before that time. You will be followed for any side effects that happen to you until you start another cancer treatment. You will continue to have tests and scans done to measure how much neuroblastoma you have left. Your doctor will tell you how often these tests will be done. We will stop checking your tumor status as part of this study if you receive another cancer therapy or if your tumor grows back.

You will remain on study for life, unless you decide to withdraw your consent. We will continue to collect information about you the rest of your lifetime regarding your health and whether you have developed any other cancer different from neuroblastoma. This information may be gotten from your oncologist or family doctor at regular intervals.

CAN I STOP BEING IN THE STUDY?

Yes. If you are thinking about stopping the study, you should talk to your doctor before making a final decision so he/she can tell you how to do this safely. There are certain time points in the study where it would be strongly recommended that you complete the medical supportive care required to avoid very bad and/or fatal side effects.

- Once you have received Ultratrace™ treatment, you will stay in the special room until you are no longer radioactive (usually 5 days), since you could expose others to radiation.
- Since all patients will receive a stem cell infusion in order for their blood counts to recover to normal levels, it would be strongly recommended that you complete the medical supportive care needed to avoid very bad and/or fatal side effects.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest; if you do not follow study rules; or if the study is stopped.

WHAT ARE THE RISKS OF THE STUDY?

This is a Phase I study. A Phase I study looks at how common and serious side effects can be for each patient at a specific dose of a drug. In a Phase I study, some patients may have very serious side effects and could die as a result of these side effects. You may be one of those patients who have serious side effects as a result of participating in this Phase I study.

In this study, researchers will be looking at side effects seen in patients taking different doses of Ultratrace™. Since Ultratrace™ subjects will be assigned to different doses of Ultratrace™, some subjects may receive a dose of Ultratrace™ that is too small to be effective while others may receive a higher dose that may cause increased side effects.

Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Other drugs may be given to make side effects less serious and more comfortable (such as for nausea, headache or itching). Many side effects go away soon after Ultratrace™, but it is always possible that side effects can be serious, long lasting or may never go away. There is also a risk of death. Patients are watched carefully throughout the study and given supportive treatments to try to prevent or resolve bad side effects that may develop. Because Ultratrace™ is a new form of MIBG has never been given to children before, there may be risks we do not know about. You should talk to your doctor about any side effects that you have while taking part in this study. While on the study, you are at risk for the side effects listed on the following pages.

Possible side effects of Ultratrace™ Iobenguane I 131

Likely	Less Likely	Rare
<p>(happens to 21-100 children out every 100 children)</p> <ul style="list-style-type: none"> • Decrease in the number of red and white blood cells and platelets made in the bone marrow. You may need blood and platelet transfusions and usually stem cell infusions are necessary. The dose of Ultratrace™ infusion used in this study may lower your blood counts. <p>Lowering the number of red blood cells, which may make you tired or pale</p> <ul style="list-style-type: none"> • Nausea • Dry mouth 	<p>(happens to 5-20 children out every 100 children)</p> <ul style="list-style-type: none"> • Decreased function of the thyroid gland. This causes tiredness (fatigue), weight gain, constipation, and lower blood pressure. Treatment for life with a medicine to supplement the thyroid gland (i.e. Synthroid or related thyroid supplement) may be needed. • Fever or infection as a result of the low white blood cells. The infection may become serious. • Fatigue from low red blood cells • Not being able to get pregnant or have a child • High or low blood pressure during Ultratrace™ infusion • Loss of appetite 	<p>(happens to < 5 children out every 100 children)</p> <ul style="list-style-type: none"> • Pain in salivary glands • Urinary tract infection from having a urinary catheter placed. (This is a risk from having a urinary catheter placed for the Ultratrace™ treatment not from the Ultratrace™ itself.) • Bruising or bleeding from the low platelet count. Bleeding can rarely become serious. • Decreased function of adrenal gland. This affects your activity level and growth. It causes tiredness (fatigue), weight changes and blood pressure changes. You may need to take medicine to supplement the adrenal gland. • Decreased heart function • Irritation of the liver and/or kidneys. Because some of the radioactive Ultratrace™ is taken up by the liver and kidneys, there is a possible risk of future liver and/or kidney damage from the Ultratrace™ alone. • Second cancer, different from the kind of cancer you have now (leukemia). • Complications related to taking Ultratrace™ may result in death <p>Dehydration</p>

Possible side effects of Potassium Iodide:

This medication is given for 45 days after the Ultratrace™ infusion, to protect your thyroid gland.

Likely (happens to 21-100 children out every 100 children)	Less Likely (happens to 5-20 children out every 100 children)	Rare (happens to < 5 children out every 100 children)
	<ul style="list-style-type: none">• Gastrointestinal distress (nausea / vomiting / diarrhea / stomach pain)	<ul style="list-style-type: none">• Tingling, pain or weakness in arms and legs• Flare up of adolescent acne• Irregular heartbeat• Confusion• Tiredness• Fever• Hypersensitivity (hives)• Burning of mouth / throat• Metallic taste• Rash• Decreased function of the thyroid gland with overuse• Swelling of lymph glands

Possible side effects of Potassium Perchlorate:

This medication is given for 5 days after the Ultratrace™ infusion, to protect your thyroid gland.

Likely (happens to 21-100 children out every 100 children)	Less Likely (happens to 5-20 children out every 100 children)	Rare (happens to < 5 children out every 100 children)
	<ul style="list-style-type: none">▪ Nausea and stomach irritation. Taking this medicine with food or meals may prevent these side effects.	<ul style="list-style-type: none">▪ Unable to make red and white blood cells, platelets▪ Hives▪ Skin rashes

Possible side effects of G-CSF (Neupogen)

G-CSF is not an anti-cancer medicine. It helps the growth of white blood cells that fight infection.

Likely (happens to 21-100 children out every 100 children)	Less Likely (happens to 5-20 children out every 100 children)	Rare (happens to < 5 children out every 100 children)
<ul style="list-style-type: none">• Bone pain	<ul style="list-style-type: none">• Pain or irritation at injection site• Increased blood tests for alkaline phosphatase, LDH and uric acid• Low platelet count• Fever	<ul style="list-style-type: none">• Allergic reactions (more common with giving the drug IV than as an injection under the skin)• Skin rash, itching, puffiness in the face• Shortness of breath or wheezing• Low blood pressure, fast heart rate• Low grade fever• Enlargement of the spleen.• Rupture of the spleen• Worsening of existing skin rashes• Sickle cell crises in patients with sickle cell disease• High white blood cell count in the blood• Irritation / inflammation of veins in the skin• Adult respiratory distress syndrome• Bone marrow dysfunction (MDS) or secondary leukemia in patients with very bad ongoing neutropenia (not as seen in cancer patients) and long term administration.

Possible side effects associated with stem cells

- **ANY TIME BEFORE STEM CELL INFUSION:** The freezer where stem cells are stored could malfunction, the container holding them could break and the stem cells could be damaged so they could not be used. This is expected to be an extremely rare event, however, if it occurs, another stem cell collection may be attempted or the back-up stem cells (if available) may be used if they were not damaged.
- If stem cells needed to be shipped from one location to another, they could be lost or damaged during shipping such that they could not be used. This is expected to be an extremely rare event. If this occurs, another stem cell collection may be attempted or the back-up stem cells, if available, may be used.
- **PURGED STEM CELLS ONLY:** Purged stem cells are treated (purged) to take out neuroblastoma cancer cells and leave the normal cells. Purging may injure the normal stem cells so they will not grow to make a normal working bone marrow after they are infused. This is expected to be an extremely rare event, but could be fatal if it happened. There is also the possible risk that purging could make the normal blood cells return back to normal numbers more slowly. There would be the option to give medicine(s) to stimulate bone marrow growth, or infuse additional back-up stem cells, if they are available.

Possible side effects of stem cell infusion

Likely (happens to 21-100 children out every 100 children)	Less Likely (happens to 5-20 children out every 100 children)	Rare (happens to < 5 children out every 100 children)
	<ul style="list-style-type: none">• Fever and chills	<ul style="list-style-type: none">• Allergic reaction. Can cause difficulty breathing and low blood pressure.• High blood pressure• Infection• Infusion of tumor cells. Tumor cells may still be present in the harvested stem cells and they could regrow after stem cells are infused.

Possible risks to unborn child

Patients who agree to participate in this study should not become pregnant while on this study. This study and the medicines used in this study may be hazardous to an unborn child. Patients and their sexual partners should use abstinence and /or an effective method of contraception that is medically appropriate based on your personal doctor's recommendation at that time.

Possible risks to the caregiver(s) of the patient getting Ultratrace™ treatment

Caregivers (example: parent, other family member, guardian, friend, sexual partner) will be exposed to radiation while you are being treated with Ultratrace™. Caregivers who could possibly become pregnant during this time need to avoid contact with the patient because the radiation exposure may increase the unborn baby's risk of developing cancer or other health problems.

If your caregiver is pregnant, then special precautions should be used to avoid contact with you during and for 4 weeks after getting Ultratrace™ treatment. Should your caregiver or your caregiver's sexual partner be found to have been pregnant while you were getting Ultratrace™ treatment and did not know it at the time, please contact your doctor immediately.

Possible long term side effects of this treatment

- Recurrence of tumor
- Infection
- Sterility and/or delayed onset of sexual maturity
- Increased risk of a second cancer (such as leukemia) different from the kind of cancer you have now.
- Patients who have Ultratrace™ treatment will receive radiation to the normal organs . It is possible that there may be later damage to the normal function of the liver, thyroid, or other organs.
- Death

Possible risks from having blood and bone marrow drawn

Blood and bone marrow will be drawn as part of your standard care. The risks from having your blood taken are minimal, but can include an infection or a blood clot. The risks of having bone marrow drawn include pain and discomfort at the site where it is taken, infection, bruising, and bleeding. Experienced doctors or nurses will perform these draws to minimize these risks. These risks will be discussed with you. You will be asked to sign a separate consent for any procedure that needs sedation such as drawing bone marrow.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

There may or may not be direct medical benefit to you. The information learned from this study may or may not benefit other children or young people with solid cancers in the future.

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

There are other options for treatment. Instead of being in this study, you may have these options, depending on what prior therapy you have received and your current medical condition. The specific options possible for you will be discussed with you by your treating doctor:

- Treatment with chemotherapy medicines without Ultratrace™.
- Treatment with the “standard” form of MIBG alone or combined with chemotherapy agents.
- Treatment with other experimental agents that may be available.
- No therapy at this time with care to help you feel more comfortable.
- Treatment with standard external beam radiation

Please talk about these options with your doctor.

WILL MY MEDICAL INFORMATION BE KEPT PRIVATE?

The following information explains how your medical health records and the research data collected about you for the study (“Protected Health Information”) may be used and disclosed. There is a federal law in the United States called the Health Insurance Portability and Accountability Act or HIPAA, which protects the privacy of Protected Health Information. It requires that research subjects receive written notification about the use and sharing of such information and that your permission is provided to the study doctor and staff to use this information in a research study. By agreeing to be in this study, you give permission for the uses and disclosures of your protected health information.

Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

You have a right to see and make copies of your medical records. To ensure the reliability of the study however you agree that you will not be able to see or copy your child’s records related to the study until the study sponsor has completed all work related to the study. At that time you may ask to see the Investigator’s files related to your participation in the study, and you may ask the Investigator to correct any study-related information about you that is wrong.

This permission to share your protected health information for this study does not have an expiration date. If you no longer want to share your protected health information, you may cancel your permission at any time by writing to the study staff and/or the Investigator. If you decide that you do not want your protected health information to be shared, then you will not longer be permitted to participate in the study and the information already collected may continue to be used and disclosed by the clinical site.

Organizations that may look at and/or copy your medical records for research, quality assurance and data analysis include:

- NANT Consortium, including NANT Data Safety Monitoring Board
- Independent auditor evaluating quality assurance for the NANT Consortium.
- The National Cancer Institute (NCI) and other governmental agencies, including the Food and Drug Administration (FDA) and Institutional Review Boards, involved in keeping research safe for people.

- Molecular Insight Pharmaceuticals, Inc., the Sponsor of this study and supplier of ULTRATRACE™ IOBENGUANE I 131 and its designees
- After the study staff or the Investigator discloses your protected health information to others, it could be re-disclosed and no longer be protected by federal privacy laws.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

Taking part in this study may lead to added costs to your insurance company. Your health insurance company will be billed for many expenses associated with the costs of this study that are considered standard of care for treatment of your neuroblastoma. These expenses include medications, treatments, hospital charges, and doctors' fees related to your participation in this study. Costs for tests and procedures that are not considered part of usual medical care and so will not be paid by insurance or governmental payors will be funded by the sponsor of this study, Molecular Insight Pharmaceuticals, Inc.

The cost of Ultratrace™ and the research tests that are not part of standard cancer care will not be billed to the patient, insurance company, or other payor. These research tests will include the MIBG scans done for dosimetry and anesthesia for these scans (if required), Holter monitor tests, and electrocardiograms.

Due to the amount of time involved in participating in this study, you will be compensated for expenses such as travel, hotel/hospital stay, meals and parking. The reimbursement amount will be evaluated on an individual basis.

Taking part in this study may lead to added costs that may be covered by your insurance company. Please ask the study doctor about any expected added costs or insurance problems.

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

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.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?

It is important that you tell your study doctor, _____ *[investigator's name(s)]*, 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 _____ *[telephone number]*.

In the event of a research-related injury, necessary medical treatment will be provided to assist your recovery from the injury. Molecular Insight Pharmaceuticals, Inc. will pay, to the extent that the treatment costs are not already covered by your primary health insurance, for any immediate medical care that is necessary to treat an injury occurring as a contemporaneous and direct result of the study. This agreement to pay for medical treatment that exceeds coverage limits of the primary policy does not apply to treatment for any pre-existing injury/illness, and any injury/illness that is not the direct and immediate result of the research. No other financial compensation will be provided.

WHAT ARE MY RIGHTS AS A STUDY PARTICIPANT?

Taking part in this study is your choice. You may choose not to take part or not take part in the study. If you decide to take part in this study, you may remove yourself from 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. If you remove yourself from the study, your study doctor will still take

care of you. We will explain what stopping the treatment may do and your study doctor will offer other treatments if they are available.

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

In case of injury resulting from this study, you do not lose any of you legal rights to seek payment by signing this form.

A Data Safety and Monitoring Board, an independent group of experts, will be reviewing data from this research throughout the study. We will tell you about new information from this Board or other studies that may affect your health or willingness to stay in the study.

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor _____ [name(s)] at _____ [telephone number].

For questions about your rights while taking part in this study, call the _____ [name of center] Institutional Review Board (a group of people who review the research to protect your rights) at _____ (telephone number).

WHERE CAN I GET MORE INFORMATION?

You may call the NCI's **Cancer Information Service** at

1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615

You may visit the NCI Web sites at <http://cancer.gov/>

For NCI's clinical trials information, go to <http://cancer.gov/clinicaltrials/>

For NCI's general information about cancer, go to <http://cancer.gov/cancerinfo/>

You will get a copy of this consent form. If you want more information about this study, ask your study doctor.

STATEMENT OF CONSENT

I have already read the information in this informed consent document. I have read all the attachments that were included with this informed consent document. I have asked all of my questions and I have gotten answers. I agree to enroll myself (my child) in this study.

Patient Name

Signature of Parent or Guardian

____/____/____
Date

Signature of Parent or Guardian

____/____/____
Date

Signature of Patient (If ≥12 years old)

____/____/____
Date

Signature of Physician or
Responsible Investigator

____/____/____
Date

Signature of Person Conducting Informed Consent Discussion

____/____/____
Date

Signature of Witness

____/____/____
Date

Signature of Translator
(If applicable)

____/____/____
Date

MEDICAL TEST CHART

A blank box means the test is not done at that time point in the study.

Tests that will be done on this study.

Observation	Before Entry	DOSIMETRY PART OF STUDY	TREATMENT PART OF STUDY	END OF THERAPY
Physical Exam	X	X	X	X
Blood Tests	X	X	At least twice/week until your blood counts recover, then at least weekly until 60 days after treatment with Ultratrace™	X
Electrocardiogram (ECG) for research purposes		X (2 ECGs)		
Holter monitor for research purposes			X	
Echocardiogram or MUGA	X			
Urine tests	X			X
Pregnancy test	X		X	X
Bone Marrow Aspirate/biopsy	X			X
CT/MRI and MIBG scans	X		X (MIBG scan only)	X
Additional MIBG scans for research purposes		X (3 scans total)		
Questionnaire	X			X