A Phase I, Open Label Study Employing the Topical Immunomodulator Diphencyprone to Treat Cutaneous Neurofibromas Associated With NF1
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STUDY INFORMATION:

Study Title: A phase I, open label study employing the topical immunomodulator diphencyprone to treat cutaneous neurofibromas associated with NF1

Study site(s): Icahn School of Medicine at Mount Sinai

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SUMMARY OF THIS RESEARCH STUDY:

This document explains a research study you might be interested in joining. Participation in the study is voluntary. You can agree to join or not. Your decision will not limit your ability to receive care at Mount Sinai. You should only agree to take part if you understand the study and if all of your questions about the research study are answered. If you do join the study, the research team must share any new information with you that may change your mind about taking part.

The purpose of this research study is to find out if diphencyprone ointment (also known as DPCP), an investigational drug that is not approved by the U.S. Food and Drug Administration (FDA), is safe and effective in treating skin growths known as neurofibromas in participants with neurofibromatosis type 1 (NF1). Neurofibromatosis type 1 is a common condition that is hereditary (spread through families). Participants with NF1 often have many growths on their skin known as neurofibromas. These growths are small (2 mm to 3 cm in size) and not cancerous, but participants with NF1 can have large numbers of them, which make them very upsetting to participants. Our body's immune system protects us from disease and infection, but unfortunately, often fails to get rid of tumors such as neurofibromas. Currently, the only way to treat neurofibromas is by cutting them out with surgery or using devices to physically destroy them. These treatments result in scars, and the neurofibromas often come back despite treatment. Therefore, we would like to assess whether the study drug DPCP, can boost your body's immune activity in the skin when it is applied topically on the skin, to fight off these growths.

If you choose to take part, you will be asked to visit with us a total of 13 times over an approximately 15 week period. The study will involve the application of various concentrations of DPCP to healthy skin on your right upper arm, left forearm, and select neurofibromas. We may take real-time images of your skin during these visits, which will be described in detail later in this document and includes medical photography, optical coherence tomography (OCT), reflectance confocal microscopy (RCM), and/or ultrasound. There are no costs to you associated with your participation in this study. You will be compensated $100 for each biopsy and $25 for each blood draw while participating in the study.

If you choose to participate, you will be asked to read and sign this consent form before any study tests are done. This study includes a screening visit (to determine your eligibility), a study treatment period (during which you will receive the study drug), and a follow-up visit (after your last dose for your safety). Each period is explained in this consent form in the order that they will be completed. This study will involve physical examinations, assessments of your neurofibromas, laboratory tests (such as blood tests and urine pregnancy tests), photographs and imaging tests of your neurofibromas, and skin biopsies (removal of a small amount of tissue for laboratory testing). Some of your blood or tissue samples may be stored. If you are eligible for this study, you will receive the study drug being tested, DPCP, which will be applied on the skin over areas of neurofibromas.

If you choose to take part, the main risks to you are mostly related to changes to the skin where DPCP is applied. Contact dermatitis (inflammation of the skin) and mild eczema similar to a poison ivy reaction along with swelling of the lymph nodes are common expected side effects. Hyperpigmentation (darkening of the skin), hypopigmentation (lightening of the skin), development of local vesiculation (fluid-filled sac), redness, and swelling may occur at sites where DPCP is applied on the skin. Fever, chills, palpitations (heart racing), flu-like symptoms, fainting spells, urticaria (hives), impaired sleep, and headaches are infrequent.

You may benefit from taking part in this research. Some potential benefits are: reduction of size or clearance of the neurofibromas from application of DPCP on the skin. The findings from this study may help to identify new therapies for addressing neurofibromas.

Instead of taking part in this research, you may decide to pursue other clinical trials or choose no treatment.

If you are interested in learning more about this study, please continue to read below.

STUDY PARTICIPATION:

You may qualify to take part in this research study because you have NF1 and at least four neurofibromas on your skin that are able to be biopsied.

Your participation in this research study is expected to last approximately 15 weeks. There will be 13 total visits that include a screening visit, treatment period (visits 2-12), and a follow up visit 30 days after the last treatment visit. The number of people expected to take part in this research study at the Icahn School of Medicine at Mount Sinai is approximately 30.

There are approximately 30 people expected to take part in this research study at the Icahn School of Medicine at Mount Sinai.

Funds for conducting this research study are provided by a research grant from the Friedman Brain Institute of Mount Sinai.

A description of this clinical trial will be available on http://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.

DESCRIPTION OF WHAT IS INVOLVED:

If you agree to take part in this research study, here is what may be involved:

In addition to the visits listed, the study doctor may ask you to come in for extra visits if necessary to protect your well-being. A description of each test, procedure, or assessment is provided in this consent.

What is going to happen in this research study?

In this study, all of the visits will occur in the Icahn School of Medicine at Mount Sinai, Department of Dermatology. There is one screening visit and then a sensitization visit in which you will receive the first dose of the study ointment on one neurofibroma, to the inner aspect of the right arm (0.4% ointment), and also to the opposite left forearm (0.04% ointment). At the Day 14 visit, it will be determined if you develop a rash at the sites that the study drug was applied to. If you do develop a rash, then you are considered sensitive to the study medication. If not, you will receive an additional dose of 0.4% of the study drug applied to a neurofibroma and be asked to return on Day 17. Since some people may not become sensitive right away, you will be asked to come to the clinic on Day 21 if sensitization is not seen at Day 17. If you are not sensitive to the drug at Day 21, you will be withdrawn from the study. If you are sensitive to the study medication, there will be an additional 11 visits to the clinic for treatment with the study medication as well as a follow-up visit. These visits may also include medical photography, ultrasound, optical coherence tomography, reflectance confocal microscopy, blood tests, and 3 skin biopsies over the course of the study. Skin biopsies will be performed on your neurofibromas. The study drug will be applied only at your clinic visit. This will occur approximately every week.

Tests and Procedures:

The following is a description of the tests and procedures involved in this study.

Informed Consent Process

At the first screening visit, you will undergo the "consent process". During this process, the purpose of the study, what will happen in the study, any possible risks and benefits, and your right to withdraw at any time will be explained in more detail. You should ask any questions you have. You will be asked to sign an Informed Consent Form to indicate that you understand the information and are willing to take part in the study. You may still ask questions, or withdraw from the study at any time during the study. Your participation is voluntary. Once you have given your consent to be in the study, you will undergo the screening process to determine if you are eligible to participate.

HIV Test

To take part in this research project we will have to test your blood for evidence of HIV infection. HIV is the virus that causes AIDS. It can be transmitted through unprotected sex (vaginal, anal, or oral sex) with someone who has HIV, and through contact with blood, as in sharing needles (piercing, tattooing, drug equipment including needles used to inject drugs). HIV-infected pregnant people can transmit to their infants during pregnancy or delivery or while breast feeding. There are treatments for HIV/AIDS that can help an individual stay healthy. Individuals with HIV/AIDS can adopt safe practices to protect uninfected and infected people in their lives from becoming infected or being infected themselves with different strains of HIV.

By law, positive test results are reported to the NYS Department of Health for epidemiological (the study of the factors determining or influencing the presence or absence of disease) and Partner Notification purposes. If you wish to be tested anonymously you will be referred to a public testing center, but you will not be able to be in this study. Please know that New York State law protects the confidentiality of HIV test results and other related information. The law prohibits discrimination based on an individual's HIV status and services are available to help with such consequences. You are free to refuse this test, but if you refuse you will not be allowed to join or remain in this research project.

Medical History and Physical Examination

A focused "medical history" and targeted "physical exam" pertinent to the study will be conducted by a medical doctor or nurse practitioner. Your vital signs (body temperature, heart rate, blood pressure, and respiratory rate) may be taken.

Lesion Measurement

An acetate sheet will be placed over your lesions and the lesions will be outlined on this paper. This is being done to determine the study drug dosing and to measure changes in the size of the lesions moving forward.

Pregnancy Test

If you are a participant that can become pregnant, you will undergo a pregnancy test which will require you to urinate into a clean dry plastic container. The staff will test your urine to see if you are pregnant.

The results of the test will be available within a few minutes. If you are pregnant, you will not be able to participate in this study.

Lesion Photography
Using digital cameras, photography of the neurofibromas will be taken. Photographs will be taken while you are standing. You will be dressed at your own comfort level. The photographs will be considered part of your personal information and we will take steps to minimize the chance that you can be recognized or identified. Every effort will be made to de-identify you to protect your privacy in your photographs. The photographs will not include your name or other identifying information associated with you. Your photographs will be treated in the same manner as study data. Please refer to the "Use of Your Data and/or Specimens" section for more details on how your study data will be handled.

Ultrasound scanning
Ultrasound scanning is used to evaluate skin thickness. It uses high-frequency sound waves to produce images of structures inside the body. You will be asked to remove all clothing and jewelry from the area being scanned. Depending on the area being scanned, you may be given a hospital gown, and you will be asked to sit or lie down on an examination table. A small amount of gel will be applied on the skin over the area to be scanned to help the sound waves move into your body. The study staff will slide the small ultrasound probe back and forth through this gel. The ultrasound instrument, also called a transducer, will transmit ultrasound waves into your body and receive their echoes. This is a painless procedure that takes about 5 minutes. You will only feel the instrument against your skin. After your scan is done, the gel will be wiped off and you will get dressed.

Optical coherence tomography (OCT)
OCT imaging is a non-invasive imaging technique similar to ultrasound. It measures echo delays to create images. In OCT, a light beam is directed at the area of interest in the skin, rather than sound or radio frequency.

Reflectance Confocal Microscopy (RCM)
RCM is a non-invasive imaging technique that uses light to achieve high-resolution images of different levels of the skin. One can think of it like a "virtual biopsy" of the skin. This is a painless procedure. First, a small amount of immersion oil is applied to the skin, and then a glass window is attached to a metal ring and placed over the oil. The glass window is fixed to the skin using medical adhesive tape to prevent skin movement. A water-based gel is placed inside the ring, which is magnetically attached to the optical lens housing of the microscope, which will then take an image.

Skin Biopsy
A biopsy refers to taking off a small area of skin using a small blade. The amount of skin taken will be 4-6 mm (0.4-0.6 cm) in diameter, approximately the size of a pencil eraser or slightly larger. Before this is done, the area will be numbed with a local anesthetic so that you will not feel pain. To close the area,

a few stitches will be placed which will be removed about two weeks later. The area will heal with a small scar. You may have as many as 3 biopsies as part of this study.

Blood test
You will have some blood drawn from a vein in your arm. These tests will be for research purposes to determine what abnormality you have in the gene that causes NF1. This will be approximately one tablespoon of blood.

Study Visits
In this part, we list what will happen at each visit you make to Icahn School of Medicine at Mount Sinai, Department of Dermatology after you have agreed to take part in this study:

Screening: 1 hour
1. informed consent process
2. medical history and physical exam
3. neurofibroma imaging
4. HIV test
5. urine pregnancy test (for participants of childbearing potential)
6. confirmation that you are eligible for this study

Day 0: 1.5 hours (must be two weeks after the screening visit for participants of childbearing potential; for other participants, this will be after HIV testing has resulted)
1. urine pregnancy test (for participants of childbearing potential)
2. neurofibroma photography and measurements
3. optional ultrasound scanning, OCT, or RCM measurement
4. possible blood draw for NF1 gene testing
5. biopsy of one of your neurofibromas
6. application of study drug (in the form of an ointment) to three different areas, one on each of your arms and one of your neurofibromas. These areas on the arms will not be biopsied and are chosen to get your body ready for the application of the study drug on Day 14.

Day 14: 1 hour (+/- 2 days)
1. if you did not respond to the drug applied on Day 0, you will have the drug application repeated on one of your neurofibromas.
2. neurofibroma photography
3. possible blood draw for NF1 gene testing
4. if you did respond to the drug applied on Day 0, you will have application of the study drug up to 20 of your neurofibromas.
5. assessment of adverse effects

Day 17: 1 hour (+/- 1 day)

1. If you were not seen to be sensitiveto the drug on Day 14, you will be checked if you are sensitiveat this visit.
2. neurofibroma photography
3. optional ultrasound scanning, OCT, or RCM measurement
4. possible blood draw for NF1 gene testing
5. If you were shown to be sensitive to the drug on Day 14, a biopsy of one of your neurofibromas treated at Day 14 will be performed.
6. assessment of adverse effects

Day 21: 1 hour (+/- 1 day)
1. If you were not seen to be sensitive to the drug on Day 17, you will be checked if you are sensitive at this visit. If you do not have a response, you will be withdrawn from the study.
2. neurofibroma photography
3. optional ultrasound scanning, OCT, or RCM measurement
4. possible blood draw for NF1 gene testing
5. if you were shown to be sensitive to the drug on Day 17, the study drug will be applied to up to 20 of your neurofibromas and the study will continue as below.
6. assessment of adverse effects

Days 28, 35, 42, 49, 56, 63, 70 (all +/- 36 hours):
1. The challenge dose of DPCP will be applied to the same neurofibromas as previously.
2. If the inflammatory response (redness and/or swelling caused by DPCP) in the skin is too strong, the topical application of DPCP will be skipped, or a lower concentration of DPCP applied, and you will return for the next visit as scheduled.
3. If the inflammatory response in the skin is too weak, an increased concentration of DPCP will be applied.
4. optional ultrasound scanning, OCT, or RCM measurement
5. possible blood draw for NF1 gene testing
6. neurofibroma photography
7. assessment of adverse effects

Day 77: 1 hour (+/- 1 day):
1. a biopsy of a neurofibroma may be performed (may be postponed to Day 107 depending on your inflammatory response to the study drug)
2. If there is extensive inflammation (redness and/or swelling) at this visit, then the biopsy will be postponed to Day 107.
3. the final dose of DPCP will be administered to neurofibromas at this visit
4. optional ultrasound scanning, OCT, or RCM measurement
5. possible blood draw for NF1 gene testing
6. neurofibroma photography
7. assessment of adverse effects

Day 107: 1 hour (+/- 1 days)
1. neurofibroma photography and measurements
2. optional ultrasound scanning, OCT, or RCM measurement
3. possible blood draw for NF1 gene testing
4. a biopsy of a neurofibroma may be performed, if not performed previously
5. assessment of adverse effects

Your active participation ends after the last biopsy is taken. All stitches will be removed 10 days to 2 weeks after any biopsies are taken during visits scheduled at your convenience. As all tissues are obtained for research purposes and not for routine clinical tests, they may be stored and used in the laboratory for many years.

In this study, you will not receive routine care for any medical conditions related to this protocol.
In this study, you will not receive routine care for any other medical conditions you may have.
Because this project involves the use of medications, it may be necessary that we make a note of your participation in the electronic medical record. That way anyone treating you will be aware of your participation and may be able to avoid any unfortunate outcomes that could arise if your research participation were unknown.

Genetic Testing

The NYS Civil Rights Law Section 79-1 covers Confidentiality of records of genetic tests. Your samples may be used for genetic tests. Genetic factors related to your skin condition will be studied. The samples and tissue obtained will be stored for as long as deemed useful for research purposes. No tests other than those authorized will be performed on the biological sample. Your results from this research will not be returned to you or your treating doctor, and will not in any way be used for treatment decisions.

HIV/AIDS

To take part in this research study, your blood will be tested for evidence of HIV, the virus that causes AIDS. People can get HIV through unprotected sexual contact with someone who has HIV, and through contact with blood (as in sharing needles including for piercing, tattooing, and injecting drugs). People who are pregnant with HIV infections can transmit HIV to their infants during pregnancy, delivery or while breastfeeding. There are treatments for HIV/AIDS that can help people stay healthy. People with HIV/AIDS can adopt safe practices to protect uninfected and infected people in their lives from getting HIV or getting infected with a different strain of HIV.

By law, positive test results for HIV/AIDS (as well as other communicable diseases such as hepatitis B, hepatitis C, and syphilis) are reported to the NYS Department of Health so they can study how people get and transmit the disease and notify sexual or needle-sharing partners they may have been exposed. If you wish to be tested anonymously for HIV/AIDS, the research team can refer you to a public testing center, but you will not be able to be in this study. New York State law protects the

confidentiality of HIV test results and other related information. It is illegal to discriminate against a person based on their HIV status and services are available to help if this happens. You are free to refuse to get an HIV test, but if you refuse you cannot be part of this research study.

Pregnancy

Since you are participating in a research study that involves an experimental treatment with unknown risks to a developing fetus, it is recommended, for your protection, that you not become pregnant for the duration of the study. You should not participate if you are breastfeeding.

If you can possibly get pregnant, a urine test for pregnancy will be done before you begin the study and the pregnancy test will be repeated at Day 0, Day 28, and Day 56.

You cannot be included in the study if you are or become pregnant, as the study drug could harm your fetus. You also should not be in the study if you are producing milk to feed a child as the study drug could harm your baby.

Unless you are at least one year past menopause or have had a successful operation to make pregnancy impossible, you should use effective birth control. Unless you are sexually abstinent (not having genital sex) the recommended methods of birth control are:

- The consistent use of approved hormonal birth control (pill, patches, or rings),
- An intrauterine device (IUD),
- Contraceptive injection (Depo-Provera),
- Double barrier methods (Diaphragm with spermicidal gel or condoms with contraceptive foam),
- Sexual abstinence (no sexual activity),
- Sterilization (a vasectomy, getting tubes tied, or a hysterectomy).

All birth control methods (other than abstinence and sterilization) are only effective if you use them properly, start them at least one month before you begin the research study, and continue using them throughout the research study and for 90 days after the research study ends. If you are unsure whether the method of birth control you use is approved to use while you are in this study, you should ask the Lead Researcher before you begin the study. If you are less than one-year post-menopausal, you could still become pregnant. If you or your partner becomes pregnant, or may be pregnant, at any time during the study, you must tell a person from the research team immediately. The team may stop the study drug and refer you/your partner to an obstetrician/gynecologist for follow-up.

Should you/your partner become pregnant, whether or not you/your partner have the baby, the people funding and overseeing the research may ask for information on the pregnancy, even if you are no

longer part of the study. You/your partner will be asked for additional written consent to share this information if that happens.

Semen/Sperm:

Drugs can be found in semen and alter sperm. Since you are taking part in a study using experimental drugs or treatments, it is recommended that 1) you use a condom, 2) you do not get a partner pregnant or expose them to semen, and 3) you do not donate semen. These recommendations apply both while you are taking the study drug, and for 90 days after you stop taking the study drug. This is because levels of the study drug may be present in the sperm and/or semen even after you stop taking the study drug. You are encouraged to tell your partner(s) and/or their doctor(s) that you are participating in this clinical trial.

USE OF YOUR DATA AND/OR SAMPLES:

The researchers would like your permission to keep your personal information (such as, name, address, date of birth, social security number), study data and/or samples (blood, tissue, urine, saliva, or any other body matter) to use or share in future studies. You can still be part of the study if you do not allow us to use or share them. Please select Yes or No to each of the questions below. To decline all future uses/sharing please select 'No' each time.

(1) Will you allow the researchers to store your data and/or samples to use in future research studies?

Please initial your choice: Yes_____ No_____

If you select No, please stop here and move to the next section, **'Your Responsibilities If You Take Part in This Research**' section below."

If yes, please continue to the next question and tell us how your personal information, study data and/or samples may be used in future research studies.

(2) The researchers can store your data and/or samples in one of two ways:

a) Anonymously (no one will know who the data and/or samples came from). If you choose this option, you can't change your mind. So, if you wanted to have your data and/or samples destroyed in the future, the team could not do it as they would not know which data and/or samples were yours.
b) Linked to your identity (using a code that can show the information came from you personally). In this case you could ask for your data and/or samples to be destroyed in the future if you want that to happen.

How would you like your data and/or samples stored? Please initial **ONE** choice below:

I would like my data and/or samples stored anonymously _____

I would like my data and/or samples stored with a link to my identity through the use of a code_____

(3) Do you give the researchers permission to keep the data and/or samples, so they could use them in future studies that are **directly related** to the purpose of the current study?

Please initial your choice: Yes_____ No_____

(4) Do you give the researchers permission to keep the data and/or samples indefinitely, so they could use them for future studies that are **not related** to the purpose of the current study (for example a different area of research)?

Please initial your choice: Yes_____ No_____

(4.1) From time to time, researchers outside of medicine and related sciences would like to use data and/or samples. This might be in the fields such as anthropology, human origins, mapping human migration patterns. Do you give permission for researchers **outside the field of medicine** to use your data and/or samples?

Please initial your choice: Yes_____ No_____

a. If the future research in a different area can be done without having to know that the data and/or samples came from you personally, that will be done.
b. If the future research in a different area requires that it is known specifically who the data and/or samples came from, then one of the following will be done:
   I. If you allowed the researchers to contact you in the future, they may be able to contact you to explain why your data and/or samples is needed and what will be done with it. Your permission will be asked to use your data and/or samples in that research project.
   II. If you do not give permission to be contacted in the future, or if it is found that contacting you is not practical (for example, because you have moved), your data and/or samples may still be used. The Institutional Review Board (IRB) will be asked for permission to use the data and/or samples linked to your identity. The IRB can give permission for researchers to use and share identifiable health information without contacting you, but only if it determines that sharing the data and/or samples will not be more than minimal risk to you or your privacy. The IRB is a committee of doctors and scientists and nonscientists, including people not associated with this hospital or medical school, whose job it is to protect people who participate in research.

(5) Do you give permission to have your data and/or samples given **to other researchers,** including those at Mount Sinai, other medical or scientific institutions and for-profit companies, for use in research within the limits you have chosen above?

Please initial your choice: Yes_____ No_____

(6) Do you give permission to have portions of your data and/or samples deposited in large public databases (repositories) for use in research with the limits you may have chosen above? Please read the paragraphs below which explains repositories, then initial your choice:

To do more powerful research, it is helpful for researchers to share data and/or samples from the people they study. They do this by putting data and/or samples into a repository. A repository is where something is stored safely for a specified period of time. Data and/or samples from one study may be stored in a repository along with data and/or samples from other studies. Sample repositories are commonly called biobanks, while data repositories are commonly called databases. . Researchers can then use the data and/or samples from multiple studies to learn even more about health and disease. If you agree to take part in this study, some of your genetic and health information might be placed into one or more scientific databases, but they will not share your direct identifiers (for example, name, address, date of birth). These databases are maintained by either Icahn School of Medicine at Mount Sinai, another institution, the federal government, or private companies. Any researcher who wants to do a study using data and/or samples from the repository must apply for permission. There are different ways of reviewing such requests. Researchers with an approved study may be able to see and use your data, along with that from many other people. Researchers may use your samples for genetic sequencing and other experimental testing. Researchers will always have a duty to protect your privacy and to keep your information confidential, but there are always risks associated with data and/or sample collection and sharing. They are described in more detail in the Risks section.

YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

If you decide to take part in this research study, you will be responsible for the following things:

- While you are taking part in this study, you should not take part in another study without notifying the study doctor.
- You must follow the instructions you are given by the study doctor and study staff. If you do not follow the instructions, your visit may have to be rescheduled, or you may be discontinued from the study.
- Tell the study doctor or the study staff about all prescription and non-prescription medications, supplements, herbal preparations, or vaccines before you take them.

- Notify the study doctor or study staff if you move and provide your new address and contact information.

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

There may be costs to you for taking part in this study. Certain safety tests or assessments may uncover underlying diseases or problems that require medical attention.

If you agree to take part in this study, you will be paid at the end of your study participation in the form of a check. You will be compensated $100 for each skin biopsy and $25 for each blood draw while participating in the study. Checks require some time to be prepared and will be given to you once processed and available.

Tax law may require the Mount Sinai Finance Department to report the amount of payment you receive from Mount Sinai to the Internal Revenue Service (IRS) or other agencies, as applicable. Generally, this happens if you receive payments that equal $600 or more from Mount Sinai in a calendar year. You would be responsible for the payment of any tax that may be due.

It is possible that products may someday be developed with the help of your data and/or samples, and there are no plans to share any profits from such products with you.

POSSIBLE BENEFITS:

There is a chance this study may benefit you, but this is not guaranteed. Others may benefit from what researchers learn from the study. Possible benefits to you include: that your neurofibromas treated by the study drug may shrink, disappear, or stop growing. The study drug may also affect similar neurofibromas that were not directly treated in the study.

POSSIBLE RISKS AND DISCOMFORTS:

There may be some risks and discomforts in taking part in this study. We know that these risks and discomforts may happen during this study:

Risks related to the Study Drug (diphencyprone or DPCP)

It is **expected** that just after the Day 0 visit you will experience some itching and skin irritation like a rash at the sites where the study drug was applied. This will last for only a few days. About 10 to 14 days after the Day 0 visit, most but not all people will experience another rash-like skin reaction with some swelling. Also after the Day 0 visit, people commonly experience lymph node swelling which is seen as swelling under the skin in areas close to where the study drug was applied.

About 2 to 3 days after the Day 14 visit, people are expected to have the sites where the study drug was applied become red and swollen and itchy. Applications of the study drug after the Day 14 visit are expected to give similar effects. Since some reactions to the study drug are expected, do not take any medications (such as Benadryl or topical ointments) or other treatments (such as ice) without consulting a study team member. Your reaction will be evaluated at your next visit or sooner if needed.

Risks include itching, localized blistering, darkening or lightening of the skin, and skin inflammation at a site far from where the drug was applied. Rare risks include fever and chills, fainting spells, disturbed sleep, flu-like symptoms, headache, feelings of an abnormal heartbeat, loss of skin color, skin rash, and hives. These risks are usually temporary and go away without treatment. More than 10,000 people have been treated with DPCP with no long-term harmful effects.

There is the risk of household members (including partners and close friends) who come in contact with the drug to become sensitized. This would result in them having a skin reaction similar to a poison ivy rash. It is important that you share this possibility with people who live with you.

Risks related to Blood drawing

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.

Risks related to Local Anesthetic

During the injection of the local anesthetic for the skin biopsy procedure, there may be a burning sensation that will last a few seconds.

Risks related to a Skin Biopsy

The risks of a skin biopsy are slight pain and slight bleeding. There may be a feeling of pressure on the skin while the biopsy is being performed. The skin biopsy will produce a small, permanent scar in the skin. Skin biopsy sites heal in a variety of ways. The final appearance will depend in part on the area of the body biopsied, the reason for the biopsy, and the underlying skin appearance before the biopsy. Scars may continue to change for many years after the sutures are removed. In addition, everyone heals differently, and it is possible that the scars may be red for some time, or become raised, darker or lighter than the surrounding skin. You will most likely have a permanent scar of some kind, and looking at your prior scars may give the best prediction of your long-term healing. An occasional person may develop a superficial, temporary wound infection at the site of the biopsy. The occurrence of any of these complications after this procedure is rare.

It is possible that your neurofibromas may not respond to the study drug and that they may spread to other parts of your body.

There may be other risks and discomforts that we do not know about now, but we will tell you about them when we know.

Risks related to loss of private information

Risk of loss of private information; this risk always exists, but there are procedures in place to minimize the risk.

Group Risks
Although your name will not be given to researchers, basic information such as your race, ethnic group, and sex may be shared. This information helps researchers learn whether the factors that lead to health problems are the same in different groups of people. It is possible that such findings could one day help people of the same race, ethnic group, or sex as you. However, they could also be used to support harmful stereotypes or discrimination.

Privacy Risks
Your name and other information that could directly identify you (such as an address, date of birth, or social security number) will never be placed into a database [if true]. However, because your genetic information is unique to you, there is a small chance that someone could trace it back to you. The risk of this happening is very small, but may grow in the future. Since the database contains genetic information, a break in security may also pose a potential risk to blood relatives as well as yourself. For example, it could be used to make it harder for you (or a relative) to get or keep a job or insurance. If your private information was misused, it is possible you would experience other harms, such as stress, anxiety, stigmatization, or embarrassment from revealing information about your family relationships, ethnic heritage, or health conditions.

Insurance Risks
There is a Federal law called the Genetic Information Nondiscrimination Act (GINA). This law makes it illegal for health insurance companies, group health plans, and most employers of over 15 people to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Additional Risks Related to Photography
You may optionally partake in whole body photography twice throughout the study period. This study procedure comes with a risk of feeling uncomfortable. There are procedures in place to minimize this risk to you. You will be dressed at your comfort level and wearing a mask and sunglasses. The amount of study members helping perform whole body photography will be minimized to the least amount possible.

OTHER OPTIONS TO CONSIDER:

You may decide not to take part in this research study. If you decide not to take part, this will not affect the clinical care you receive at Mount Sinai. The choice is totally up to you.

Instead of being in this research study, your choices may include: treatment of the lesions with another therapy including surgical removal, laser treatment, or other experimental therapies.

IN CASE OF INJURY DURING THIS RESEARCH STUDY

If you are injured or made sick from taking part in this study, you will get medical care. The group funding this research study will pay you for any reasonable and necessary medical expenses to diagnose and treat research-related injury or illness. This does not prevent you from seeking payment for injury related to malpractice or negligence. You can contact the Lead Researcher for more information.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this study at any time. No matter what you choose, your care and benefits through Mount Sinai will not be negatively impacted.

If you decide to stop being in the study, please contact the Lead Researcher or the research staff. For your safety, once you stop the study drug you will be asked to complete the end of treatment visit and are permitted to be seen for a follow-up visit.

You may also withdraw your permission for the researchers to use and share any of your protected information for research, but you must do so in writing to the Lead Researcher at the address on the first page. Even if you withdraw your permission, the Lead Researcher may still use the information that was already collected if that information is necessary to complete the research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from taking part in the research study.

If you decide to stop being in the research study, the following may occur: any improvements in your neurofibromas may be lost or the neurofibromas may worsen.

If you stop being in the research study, the research team may not remove information they have already placed in the study database, and may continue to use that data as part of this study. The research team may ask you whether they can continue to collect information from your medical record. If you agree, this data will be handled the same as research data.

If you decide you don't want your data and/or samples to be used for research anymore, you can contact the researcher and ask to have your data and/or samples withdrawn or labeled so that they will not to be used in additional projects or shared. If your data and/or samples have already been shared with researchers, those researchers will be asked to stop using them. However, if any data and/or samples have already been shared without your identity or a linking code, it won't be possible to retrieve them. Data and/or samples that have already been used will not be affected by your decision. If your data and/or samples have already been deposited in an external repository, the study team will request that your data and/or samples be removed.

Withdrawal without your consent: The Lead Researcher, the funder or Mount Sinai may stop your involvement in this research study at any time without your consent. This may be because the research study is being stopped, the instructions of the research team have not been followed, the Lead Researcher believes it is in your best interest, or for any other reason. If data and/or samples have been stored as part of the research study, they too can be destroyed without your consent.

CONTACT INFORMATION:

If you have any questions, concerns or complaints at any time about this research, or you think the research has harmed you, please contact the office of the research team and/or the Lead Researcher at phone number 212-241-3288.

If there is an emergency, please call 911 or go to the emergency room. Let the emergency room staff know you are in a research study so they can contact the Lead Researcher if needed.

DISCLOSURE OF FINANCIAL INTERESTS:

Researchers sometimes get paid for consulting or doing work for companies that produce drugs, biologics or medical devices. If you have questions regarding industry relationships, you are encouraged to talk to the Lead Researcher or visit our website at http://icahn.mssm.edu/ where Mount Sinai publicly discloses the industry relationships of our faculty.

The company sponsoring this research study is Mount Sinai, through a research grant provided by Mount Sinai's Friedman Brain Institute. Hapten Pharmaceuticals, LLC, the company that manufactures the drug being tested, is not sponsoring this research study, but will be providing the study drug and so has a financial interest that could be affected by the outcome of this research study.

MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

As part of this study, some of your private and/or protected health information will be obtained, used, and shared with your permission. There is a Federal Health Insurance Portability and Accountability Act (HIPAA) that makes sure this is done correctly and safely.

What is protected health information (PHI)?
PHI is the combination of two things:

1. PHI contains information that identifies you. It will be used to contact you and link you to your health information, like name, date of birth, medical record number, and address.
2. PHI also contains health information, including information about your mental and physical health from your visits to doctors or hospitals, or from study visits.

Every time you visit a hospital or your doctor, PHI is created and recorded in your medical record by your healthcare providers. In the same way, the PHI created as part of this study will be linked to who you are and your medical information.

What PHI is collected and used in this research study, and might also be shared with others?

As part of this study, the research team at the hospital(s) involved in the research will collect your name, address, telephone/fax numbers, dates directly related to the individual (birth, admission, discharge, date of death, etc.), e-mail, social security number, medical records number, photographic images.

During the study, the researchers will gather information by:

- Reviewing and/or taking your medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)
- Doing a physical examination that generally also includes blood pressure reading, heart rate, breathing rate, and temperature.
- Completing the tests, procedures, questionnaires and interviews explained in the description section of this consent.
- Reviewing HIV-related information, which includes any information indicating that you have had an HIV-related test, or have HIV infection, HIV-related illness or AIDS, or any information which could indicate that you have been potentially exposed to HIV.
- Reviewing genetic tests.

Why is your PHI being used?
Researchers need the information that identifies you so they can contact you during the study. They need your health information and the results of any tests and procedures being collected as part of this study to answer the questions posed in the study. The purpose of the study is discussed earlier in this consent form. Before researchers analyze the data, they remove any information that would let others know who you are or that you took part in the study. If researchers publish or present study results at scientific meetings, lectures, or other events, their presentations would not include any information that would let others know who you are, unless you give separate permission to do so.

The Lead Researcher may also use and share the results of these tests and procedures with other healthcare providers at Mount Sinai who are involved in your care or treatment. The research team and other authorized members of The Mount Sinai Health System (“Mount Sinai”) workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example:

- The Mount Sinai Program for the Protection of Human Subjects is responsible for overseeing research on human participants and may need to see your information.

- If you receive any payments for taking part in this study, the Mount Sinai Finance Department may need your name, address, social security number, payment amount, and related information for tax reporting purposes.
- I*f the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.*

Who, outside Mount Sinai, might receive your PHI?
As part of the study, the Lead Researcher, research team and others in the Mount Sinai workforce may disclose your PHI, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Lead Researcher.)

- The United States Department of Health and Human Services (DHHS) and the Office of Human Research Protection (OHRP) (the government organization that is responsible for protecting human research participants).
- Mount Sinai laboratories who will be performing laboratory analysis for our research center.
- The IRB overseeing this study: The Program for the Protection of Human Subjects
- The United States Food and Drug Administration

In all disclosures outside of Mount Sinai, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law. Some records and information disclosed may be identified with a unique code number. The Lead Researcher will ensure that the key to the code will be kept in a locked file, or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the law requires it, or rarely if the Institutional Review Board (IRB) allows it after determining that there would be minimal risk to your privacy. It is possible that a sponsor or their representatives, a data coordinating office, a contract research organization, may come to inspect your records. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers. Additionally, when applicable, the monitors, auditors, the IRB, *OHRP, as well as the Food and Drug Administration (FDA) will be granted direct access to your medical records for verification of the research procedures and data. OHRP and FDA are authorized to remove information with identifiers if necessary to complete their task. By signing this document you are authorizing this access.* The results of this research may be published. However, your name and other identifying information will be kept confidential.

For how long will Mount Sinai be able to use or disclose your PHI? Your authorization for use of your PHI for this specific study does not expire.

Will you be able to access your records?

During your participation in this study, you will have access to your medical record and any study information that is part of that record. The research team is not required to release research information to you that is not part of your medical record.

Do you need to give the researchers permission to obtain, use or share your PHI?
NO! If you decide not to let the research team obtain, use or share your PHI, you should not sign this form, and you will not be allowed to volunteer in the research study. If you do not sign, it will not affect your treatment, payment, or enrollment in any health plans or affect your eligibility for benefits.

Can you change your mind?
If you decide to stop being in the study, please contact the Lead Researcher or the research staff. The research team may ask you whether they can continue to collect information from your medical record. You will also have to decide if you wish to limit the continued use of the information collected during the study. Under US privacy laws you may also withdraw your permission for the researchers to use and share any of your protected information for research, but you must do so in writing to the Lead Researcher at the address on the first page.

Even if you withdraw your permission, the Lead Researcher may still use the information that was already collected, but only to complete this research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from taking part in the research study.

If you have not already received it, you will also be given The Hospital's Notice of Privacy Practices that contains more information about how The Hospital uses and discloses your PHI.

It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection regulations. However, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

If researchers are reviewing your medical records or asking questions about your medical history or conditions, it is possible that they may learn information related to your HIV status. If that is the case, the following information concerns you. If researchers are not reviewing your medical records or asking questions about your medical history or conditions, then you may ignore the following section.

Notice Concerning HIV-Related Information
If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human

Rights at (888) 392-3644 or the New York City Commission on Human Rights at (212) 416-0197. These agencies are responsible for protecting your rights.

How the Institutional Review Board (IRB) can help you:

This research has been reviewed and approved by an Institutional Review Board (IRB). You may reach a representative of the Mount Sinai Program for Protection of Human Subjects at telephone number (212) 824-8200 during regular work hours (Monday-Friday, 9am-5pm, excluding holidays) for any of the reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System:

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

ADULT PARTICIPANT:

Your signature below documents your permission to take part in this research study and to the use and disclosure of your protected health information. A signed and dated copy will be given to you.

Signature of Participant	Printed Name of Participant	Date	Time
_____	_____	_____	_____

PERSON EXPLAINING STUDY AND OBTAINING CONSENT:

Signature of Consent Delegate	Printed Name of Consent Delegate	Date	Time
_____	_____	_____	_____

WITNESS SECTION:

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the participant, and that consent was freely given by the participant.

Signature of Witness	Printed Name of Witness	Date	Time
_____	_____	_____	_____