INFORMED CONSENT TO TAKE PART IN A RESEARCH STUDY

TITLE:	A 24-Week Open-Label Study Evaluating the Efficacy and Safety of OPN-375 186 µg Twice a Day (BID) in Adults with Bilateral Nasal Polyps using Nasoendoscopic Video
PROTOCOL NO.:	OPN-FLU-NP-3104 WIRB® Protocol #20180279
SPONSOR:	OptiNose US, Inc
INVESTIGATOR:	Name Address City, State Zip Country
STUDY-RELATED PHONE NUMBER(S):	Name Number(s) (24-hour phone number required)

What is the purpose of this form?

You are being asked to participate in a research study. It is important that you read the following explanation of the proposed procedures. This form describes the purpose, procedures, benefits, risks, discomforts and precautions of the study. It also describes the alternative procedures that are available to you and your right to withdraw from the study at any time. A member of the study staff will read through the consent with you and discuss all the information. When you think you understand the study, you will then be asked if you agree to take part. If you agree, you will be asked to sign this consent form. Once you sign it, we will give you a signed and dated copy to keep.

You may show this consent form to family, other doctors, and friends before you sign it. You may want to discuss it with them to help you decide if you want to be part of the study. If you do not know another doctor, but want a second opinion about this study, please ask. The study doctor will give you the name of another doctor that you can talk to.

You are being asked to participate in this study because you have been diagnosed with nasal polyps in both sides of your nasal cavities.

Why is this study being done?

This study is being conducted to see if OPN-375 (fluticasone propionate nasal spray with an exhalation delivery system that delivers drug into the nose) is safe and effective in reducing your nasal symptoms and the size of your nasal polyps, and to provide video evidence of the changes that occur over time with OPN-375 treatment. The sponsor will pay the study doctor for conducting this study and for your participation.

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

What is being studied?

Currently, the most commonly used medications for the treatment of nasal polyps and their symptoms are part of a class of medications called corticosteroids. Corticosteroids are natural substances found in the body that help fight inflammation. Fluticasone propionate is a man-made corticosteroid.

Fluticasone propionate given at a dose of 186 mcg twice a day using the exhalation delivery system is being used in this study. This study seeks to document the response of your polyps by documenting the change in the size of your nasal polyps, and to provide video evidence of the changes that occur over time. The documentation of polyp change over time is not done routinely and is therefore considered investigational.

OPN-375 (fluticasone propionate) is approved by the FDA as XHANCE™ for the treatment of nasal polyps in adults. The approved doses are one or two sprays per nostril twice daily (total daily dose of 372-744 micrograms).

The delivery system has a nose piece and mouthpiece and a glass bottle that contains the study medication. The user administers the medication by inserting the nosepiece into one nostril and the mouthpiece into the mouth. The user then blows forcefully into the mouthpiece while pushing up on the bottom of the glass bottle. The medication then flows into the nasal cavity. The procedure is repeated in the other nostril. You will use the study medication twice a day, in the morning and at night. You will receive detailed instructions on the number of sprays and how to properly use the device.

What do you need to know about this study?

Approximately 10 patients are expected to take part in this study at 2 US sites. The entire study is expected to last for about 24 weeks. Your participation in the study will last up to 24 weeks.

What will happen during this study?

PROCEDURES TO BE FOLLOWED DURING THE STUDY

Visit 1 (Day 1/Baseline)

If you decide you want to be in the study, you will have the following procedures, called "screening procedures," performed to find out if you qualify to be in this study. This visit will last about 2 hours.

- The study staff will review with you your medical history including a review of your current medications. You will not be permitted to take or use certain medications while you are in the study. It is important that you inform your study doctor or research staff of <u>all</u> prescription and nonprescription medications, dietary supplements and vitamins which you are presently taking or have taken within the past 1 month. If you have asthma or chronic obstructive pulmonary disease (COPD) you will be asked about medications, you have taken within the past 3 months.

- The study staff will review inclusion/exclusion criteria (study rules) with you.
- You will receive instruction on the use of OPN-375. You will be given a training device that contains no active medication and the study staff will evaluate your ability to correctly use the device. You will return the training device to the study staff.
- If you are a woman who can have children, a urine pregnancy test will be performed. If you are pregnant (test positive) you will not be allowed to participate in the study.
- Your vital signs (blood pressure and heart rate) will be measured.
- You will complete a questionnaire that consists of 22 questions related to the symptoms of and how you feel about your nasal polyps. This questionnaire takes less than 5 minutes to complete
- A test for your sense of smell will also be conducted. You will smell, either blindfolded or with open eyes, pens with different odors. The substances used are all non-toxic and not harmful in the concentrations given. If you are unable to smell and cannot decide on an answer, please use your best guess. There are three parts to the test which will take about a total of 30-40 minutes to complete.
- A nasal examination will be performed and a nasoendoscopy will be performed using a nasoendoscope. The nasoendoscope is a long thin tube with a bright light at the end. It allows your doctor to look at the nasal passages and other surrounding structures. This procedure is done with you sitting in a chair with a head support. Your doctor will decide if you will require the use of a local anesthetic (applied directly to the area) and / or a decongestant before the nasoendoscopy is performed. Your doctor will insert the endoscope into your nostril(s) and through the nasal passages. Your doctor will observe, record, and grade the nasal polyps that are present, and will record the nasal examination. An independent doctor will also grade the polyps based on the video recording of the nasal examination. The video recording viewed by the independent doctor will not have your name on it.

If you qualify for the study after screening procedures during the Day 1/Baseline visit, you will be given a 3-month supply of the study medication and your study staff will review the proper use of the device with you. You will give yourself morning and evening doses of the study medication as directed by the study team and the instructions provided.

At each visit you must bring back your study medication.

Study Staff will contact you approximately every 4 weeks between site visits to confirm if you are taking your medication as instructed, to inquire if you have had any changes in your health and to record changes in your medications since your last visit.

Visit 2 (Week 12)

At this visit the study staff will ensure that you are still eligible to continue participating in the study. This visit will last about 2 hours.

- Your study team will review any changes in your health and changes in your medications since your last visit.
- If you are a woman who can have children, a urine pregnancy test will be performed; you will be told if you are pregnant and will not be able to continue your participation in the study.
- Your vital signs (blood pressure and heart rate) will be measured.
- You will complete a questionnaire that consists of 22 questions related to the symptoms of and how you feel about your nasal polyps. The questionnaire takes approximately 5 minutes to complete

- You will complete a questionnaire about your overall impression of the changes in your symptoms that takes less than 5 minutes to complete
- A nasal examination will be performed and a nasoendoscopy will be performed using a nasoendoscope. The nasoendoscope is a long thin tube with a bright light at the end. It allows your doctor to look at the nasal passages and other surrounding structures. This procedure is done with you sitting in a chair with a head support. Your doctor will decide if you will require the use of a local anesthetic (applied directly to the area) and / or a decongestant before the nasoendoscopy is performed. Your doctor will insert the endoscope into your nostril(s) and through the nasal passages. Your doctor will observe and record the nasal polyps that are present, including a video recording of the nasal examination. An independent doctor will also grade the polyps based on the video recording of the nasal examination. The video recording viewed by the independent doctor will not have your name on it.
- Your study staff will review the proper use of the device with you.
- You must bring back your study medication and you will receive new medication.

Study Staff will contact you approximately every 4 weeks between site visits to confirm if you are taking your medication as instructed, to inquire if you have had any changes in your health and to record changes in your medications since your last visit.

Visit 3 (Week 24)

During this visit the following procedures will be performed. This visit will last about 2 hours.

- Your study team will review any changes in your health and changes in your medications since your last visit.
- If you are a woman who can have children, a urine pregnancy test will be performed; you will be told if you are pregnant.
- Your vital signs (blood pressure and heart rate) will be measured.
- You will complete a questionnaire that consists of 22 questions related to the symptoms of and how you feel about your nasal polyps. The questionnaire takes approximately 5 minutes to complete.
- You will complete a questionnaire about your overall impression of the changes in your symptoms that takes less than 5 minutes to complete
- A test for your sense of smell will also be conducted. You will smell, either blindfolded or with open eyes, pens with different odors. The substances used are all non-toxic and not harmful in the concentrations given. If you are unable to smell and cannot decide on an answer, please use your best guess. There are three parts to the test which will take about a total of 30-40 minutes to complete.
- A nasal examination will be performed and a nasoendoscopy will be performed using a nasoendoscope. The nasoendoscope is a long thin tube with a bright light at the end. It allows your doctor to look at the nasal passages and other surrounding structures. This procedure is done with you sitting in a chair with a head support. Your doctor will decide if you will require the use of a local anesthetic (applied directly to the area) and / or a decongestant before the nasoendoscopy is performed. Your doctor will insert the endoscope into your nostril(s) and through the nasal passages. Your doctor will observe and record the nasal polyps that are present, including a video recording of the nasal examination. An independent doctor will also grade the polyps based on the video recording of the nasal examination. The video recording viewed by the independent doctor will not have your name on it.
- You will return your study medication.

What is being performed specifically for the study?

The following are being performed for the purposes of this study and are not considered standard care:

Urine Pregnancy tests (for women who can become pregnant), additional office visits, completion of questionnaires and the smell tests.

Other Important Information/ Participant Responsibilities

If you decide to take part in this research study, you will be expected to complete the study visits and other procedures and to follow the instructions of the study doctor and study staff. It is important that you follow the study doctor's instructions for taking the study medication and that you do not give the study medication to anyone else.

If you require a reading aid to read/write (e.g. glasses), kindly ensure that you bring such aids with you to all study visits, to assist with the completion of the questionnaires.

During your participation in the study you will receive your assigned study medication for the time that you are actively participating in this research study; however, the study medication will not be made available to you after your participation in this research study ends.

If you decide to stop participating in the study, it is important that you notify the study doctor or study staff. You will be asked to return to the study center for a final study visit.

What are the potential risks of being in the study?

UNKNOWN RISKS TO PREGNANT WOMEN, EMBRYO, FETUS OR NURSING INFANT

Use of the study medication may involve unknown risks to a pregnant woman, an embryo, fetus (unborn baby), or nursing infant. Therefore, if you are pregnant, planning to become pregnant or are lactating (including breastfeeding a child), you cannot participate in this study.

If you are a woman who could become pregnant, you must either be abstinent (not have sexual intercourse) or you must use birth control during your study participation. The following methods of birth control are acceptable during participation in the study:

- prescription oral contraceptives (the Pill),
- contraceptive injections,
- contraceptive patch,
- intrauterine device,
- double-barrier method defined as condoms, diaphragm, or cervical cap with spermicidal foam, cream, or gel (the cervical cap, even with spermicidal foam, cream or gel is not as effective as other options),
- or female study participants whose male partner is sterile.

If you are postmenopausal, but for less than 1 year, meaning that you have had menstrual bleeding within the 1 year before entry into this study, you will be required to have pregnancy tests and must use birth control if sexually active.

Your study doctor will discuss with you whether the methods of birth control you plan to use are acceptable for this study.

Before entering the study, a urine pregnancy test will be done for all women who are able to become pregnant. This test might not detect an early pregnancy. Urine pregnancy tests will be repeated at each office visit. If you think you are pregnant, tell the study doctor immediately.

Pregnancy will be a reason to stop study treatment. If you become pregnant during the study, you will be discontinued from study participation for safety reasons. If you become pregnant, please make your obstetrician aware of your study participation.

POSSIBLE SIDE EFFECTS OF OPN-375

Nose Problems

Nose problems may include: nose bleeds, sores (ulcers) in your nose, a certain fungal infection in your nose, mouth, and/or throat (thrush), and hole in the cartilage of your nose (nasal septal perforation). Symptoms of nasal septal perforation may include: crusting in the nose, nose bleeds, runny nose, and whistling sound when you breathe.

Slow Wound Healing

The use of fluticasone may slow wound healing in your nose. You should let the study doctor know if you have a sore in your nose, have had surgery on your nose, or if your nose has been injured.

Eye Problems

Glaucoma and cataracts have been reported with long term use of corticosteroids. You should let the study doctor know if you have any eye problems and if you experience any change in your eyesight.

Serious Allergic Reactions

You should let your study doctor know or get emergency medical care (call 911 or go to the nearest emergency room) if you get any of the following signs of a serious allergic reaction: rash, hives, swelling of your face, mouth, and tongue, and breathing problems. These reactions might become very serious and even life-threatening. If you have a history of hypersensitivity to any medications you should let your doctor know so s/he can decide if it is safe for you to participate in this study.

Weakened Immune System and Increased Chance of Getting Infections (Immunosuppression)

Taking corticosteroids such as fluticasone propionate may make you more likely to get infections and can make certain infections worse. These infections may include tuberculosis (TB), ocular herpes simplex infections, and infections caused by fungi, bacteria, viruses, and parasites. Avoid contact with people who have a contagious disease such as chickenpox or measles while using OPN-375. If you meet someone who has chickenpox or measles call your study doctor right away. Symptoms of an infection may include: fever, pain, aches, chills, feeling tired, nausea, vomiting.

Reduced Steroid Hormone Levels (adrenal insufficiency).

Adrenal insufficiency happens when your adrenal glands do not make enough steroid hormones. This can happen when you stop taking oral corticosteroid medicines (such as prednisone) and start taking medicine containing a topical steroid (such as OPN-375). Symptoms of adrenal insufficiency may include: feeling tired, lack of energy, weakness, nausea and vomiting, and low blood pressure.

Bone Thinning or Weakness (Osteopenia or osteoporosis)

Most Common Side Effects

The most common side effects of OPN-375 include: nose bleeds, redness or sores (ulcers) in the nose, nasal congestion, headache, sinus infection, sore nose and throat, and sore throat.

Drug interactions with Fluticasone

Certain medications may interact with OPN-375. It is important that you inform your study doctor or research staff of all medications you are currently taking.

Other possible discomforts from participating in this study

The nasal endoscopy may activate the gag reflex (i.e. make you feel like you are choking or going to vomit). Nosebleed, nasal discomfort, spasms, and cough may also occur. Let your doctor know if you are experiencing any unpleasant symptoms during the procedure.

Will you be informed of new information relating to the study?

All new findings discovered during the course of this research study that may reasonably influence your decision to continue to participate in this study will be provided to youby your study doctor as such information become available.

Does being in this study provide any benefit?

Participating in this study may or may not provide a direct benefit to you. It is hoped that the information learned in this research may benefit future patients with nasal polyps.

Who do you contact in the event of an emergency?

If you suffer any medical events that are not typical for you during this study, the events would be considered an “adverse event”. Adverse events are not necessarily side effects of the study medication. For example, a person might have an upset stomach due to receiving a study medication, or the upset stomach might occur without the study medication. We will watch everyone in the study for any adverse events.

You will be monitored very closely by the study doctor and medical staff while you are in the study. This monitoring will include vital signs, nasal examinations, and other tests if the study doctor feels that they are needed.

It is important that you tell the study staff if you feel abnormal or unusual in any way. If you are not completely truthful about any side effects, you may increase the risk of harming yourself by taking part in this study. You will be given any new information that may affect your willingness to start or continue in the study.

If you experience an adverse reaction or a research-related injury during the course of the study, you should immediately contact Dr. [Name] at [Number] or [Number] (if during non-business hours).

If you seek emergency care, or if you are hospitalized, please alert the doctor who is treating you that you are enrolled in a research study being conducted by Dr. [Name].

What happens if you have a research related injury?

If you suffer a physical injury as a result of your participation in this study, you will be reimbursed for medical expenses to treat the injury, to the extent not paid by your insurance or if you do not have insurance. You may receive medical care in the same way as you would normally. No funds have been set aside for payments or other forms of compensation (such as for lost wages, lost time, or discomfort). However, you do not give up any of your legal rights by signing this consent form.

What other treatments are available?

Alternative Treatments

Your alternative to taking part in this study is to receive standard medical care as prescribed by your doctor. The following treatments are available for nasal polyps:

- nasal corticosteroid spray
- oral corticosteroids such as prednisone
- Sometimes, nasal polyps are so large and obstructive that corticosteroid nasal sprays are ineffective. In such cases, surgery can be an effective option.

Your study doctor will be able to discuss alternative procedure(s) or treatment(s) that may be available, and their potential benefits and risks.

Will it cost you anything to be in this study?

The study medication will be made available to you at no charge and you will not pay for any protocol-related tests and procedures during your participation in the study. You and/or your insurance provider may be billed for any standard medical care that is not part of this research study.

Will you be paid for being in this study?

To help defray any costs associated with your participation (for example, travel costs), you will be paid $50.00 per each completed visit up to a total of $150.00 for completing the entire study. If you should not complete the study, you will be paid for each of the visits you have completed.

The Investigator/Study doctor will receive compensation from the Sponsor to conduct this research study.

Do you have to be in this study?

Your participation in this study is voluntary. Your refusal to participate or your withdrawal from the study will involve no penalty or loss of benefits to which you are entitled. You may stop your participation at any time without affecting your ongoing medical care. If you decide to stop participating in the study, it is important that you notify the study doctor or study staff. You will be asked to return to the study center for a final study visit.

Can you be removed from the study without your permission?

Your study doctor may end your participation in this study for any of the following reasons:

1. If you develop a side effect or medical condition that may place you at risk of further complications by continuing your participation or if you need a medicine not allowed on this study;
2. If you become pregnant;
3. If you are unable to take the study medication
4. If you are unable to keep your scheduled appointments;
5. If the study is cancelled by the sponsor, the Institutional Review Board/ Ethics Committees, FDA or any other Regulatory Authority.
6. For administrative reasons.

Who will have access to your study and/or medical information?

Records of your participation in this study will be held confidential except as disclosure is required by law or as described in this informed consent document. Disclosures required by law may include: suspected child abuse; infectious disease; expression of suicidal ideas; those situations in which research documents are ordered to be produced by a court of law; and those situations in which researchers are required to report to the appropriate authorities. The study doctor, the sponsor or persons working on behalf of the sponsor and under certain circumstances, representatives of the FDA, Institutional Review Board (IRB), and other Regulatory Authorities will be able to inspect and copy confidential study-related records which identify you by name. Therefore, absolute confidentiality cannot be guaranteed. If the results of this study are published or presented at meetings, you will not be identified.

Who do you contact if you have questions about the study?

Your study doctor will answer any questions regarding OPN-375, fluticasone propionate, its risks, side effects, potential benefits, and other treatment options available to you now or at any time you are taking part in this study.

PRIVACY: COLLECTION, USE AND DISCLOSURE OF IDENTIFIABLE PRIVATE HEALTH INFORMATION

During your participation in this research study, the study doctor and study staff will collect or create personal health information, such as documentation of medical histories, physical examination, etc., about you. The study doctor will keep this personal health information in your study-related records. In addition, the study doctor may obtain, and include in your study-related records, information about your past, present and/or future physical or mental health and/or condition. (Your study doctor may ask you or your legally acceptable representative to sign a separate consent/release to obtain some or all of your medical records from your doctor(s) or other healthcare provider(s).) Your study-related records may include other personal information, medical record number(s), or any other identifying health information number, initials, date of birth, etc., that could be used to identify you. (Health information that contains information that can be used to identify you will be called “Identifiable Private Health Information” or “IPHI.”).

The IPHI to be collected, used and disclosed during this study includes: physical examinations, medical history and other data collected during this study.

If you do not agree to share your IPHI you will not be able to participate in this study. By signing this consent document, you are giving the study doctor permission to disclose your IPHI to:

- The sponsor of this study and anyone working on behalf of the sponsor to conduct this study ("sponsor'). The sponsor will analyze and evaluate the data that may contain your IPHI and may use it to develop new tests, procedures and commercial products. The study staff will assign a code number and/or letters to your study-related records which mean that you will not ordinarily be identified in the records sent to the sponsor. The sponsor may, however, look at your complete study records that identify you. In addition, the sponsor may visit the study site to oversee the way the study is being conducted and may review your IPHI during these visits to make sure the information is correct.
- The Institutional Review Board ("IRB") may have access to your IPHI in relation to its responsibilities as an Institutional Review Board.
- Clinical monitors and auditors, who work for the study sponsor, will have access to all information about you at the study site, so that they can verify the information. Also, the study sponsor might review or copy all your records, including the above information, to assure the quality of the study or for other uses allowed by law.

The study doctor or sponsor may disclose your IPHI to the FDA and/or similar government agencies in other countries.

Except for the disclosures described above, your IPHI will not be shared with others unless disclosure is otherwise required by law, for example, if a court of law orders the disclosure. If you have questions about this, please ask the study doctor.

Your consent to collect, use and disclose IPHI will expire fifty (50) years from the date you sign it unless you cancel it sooner. You can cancel your consent to collect, use and disclose your IPHI at any time. To do so, you must write a letter to the study doctor stating that you are revoking your consent to collect, use and disclose your identifiable private health information. If you cancel your consent allowing the study doctor to collect, use and disclose your IPHI, you will not be allowed to continue in the study. The study doctor will no longer use or share your IPHI unless it is necessary to protect the integrity of the study.

There are national and provincial/territorial laws that require the study doctor to protect the privacy of your IPHI; however, there is no guarantee of absolute privacy because of the need to share information. After disclosure of your IPHI, the laws may no longer protect the privacy of your information. The sponsor or others may share your information with other people who are not required to protect the privacy of your information.

If you would like to know how the sponsor will protect the privacy of your records, ask the study doctor how to get this information.

You have a right to see and make copies of your study-related information. By signing this consent document, however, you agree not to see or copy some or all your records until the sponsor has completed all work related to this study. At that time, you may ask to see your records.

VOLUNTEER'S STATEMENT:

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. I may contact Dr. [Name] at the phone number listed above on the first page if I have any more questions, concerns, or complaints about taking part in this study. I understand that Dr. [Name] or the company he/she is employed by is being paid by the sponsor for my participation in this study.

I understand that my participation in this research project is voluntary. I know that I may quit the study at any time without harming my future medical care or losing any benefits to which I might be entitled. I also understand that the investigator in charge of this study may decide at any time that I should no longer participate in this study.

This study has been reviewed and approved by the Western Institutional Review Board® (WIRB®). If you have any questions, concerns or complaints about this study, or questions about your rights as a research participant-, or the Investigator's responsibilities, you may contact WIRB 24 hours per day and 7 days per week at 360-252-2500 or toll-free at 1-800-562-4789. An IRB is a group of scientific and non- scientific individuals who perform the initial and ongoing ethical review of the research study with the subject's rights and welfare in mind. If you have any study-related comments, complaints or concerns, we ask that you first contact the study investigator. Please call the IRB if you need to speak to a person independent from the Investigator and the research staff, and/or if the Investigator and the research staff could not be reached.

By signing this form, I have not waived any of my legal rights.

I have read and understand the above information. I agree to participate in this study. I understand that I will be given a copy of this signed and dated form for my own records.

Printed Name of Study Participant	Signature of Participant	Date
Printed name of the person explaining the consent	Signature of person explaining the consent	Date
Printed name of Investigator	Signature of Investigator	Date