Approved: 05Feb2018

INFORMED CONSENT FORM AND HIPPA AUTHORIZATION

Protocol Title:	A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Fasinumab in Patients with Moderate-to-Severe Chronic Low Back Pain and Osteoarthritis of the Hip or Knee
Protocol Number:	R475-PN-1612
Sponsor's Information:	REGENERON PHARMACEUTICALS, INC. 777 OLD SAW MILL RIVER ROAD TARRYTOWN, NY 10591
Study Doctor Name:	**Michael Giovanniello MD**

Research Site Address(es):

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Physicians' Research Options,
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Daytime Telephone Number(s): 801-676-7627 and Research Office: 801-352-9228

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Introduction
You are being asked to participate in a research study of the investigational drug, fasinumab, for the treatment of chronic moderate-to-severe low back pain in patients who have osteoarthritis (OA) of the hip or knee. While patients are also required to have OA, the Sponsor (Regeneron) is conducting this study to determine how effective and how safe fasinumab is for the treatment of chronic moderate-to-severe low back pain compared to placebo (an inactive substance).

Fasinumab is an investigational drug. This means that it is not approved in your country for use in pain management by the United States Food and Drug Administration (FDA).

You are eligible for the study if you have chronic low back pain and have a history of:

1) Inadequate pain relief from non-medication therapy (eg, physical therapy)
2) Inadequate pain relief from acetaminophen/paracetamol (examples: Tylenol® or Atasol®) AND
3) Intolerance to or inadequate pain relief from at least one oral non-steroidal anti-inflammatory drug (NSAID) (examples: Motrin®, Advil®, Voltaren®, Mobic®, Naprosyn®, Celebrex®) AND
4) Intolerance to or inadequate pain relief from at least one opioid or tramadol (examples: Fentanyl® and Ultram®). If you are unwilling to take opioids or tramadol or do not have access to this type of medication you also may be eligible

You may be eligible to participate in this research study.

You need to:

1. Read this entire document,
2. Understand the information within the document, and
3. Upon the acknowledgement of your understanding, sign your name to this document if you would like to take part in the study.

Once you sign this document, a copy will be given to you and you can participate in the study as long as you meet all the study conditions.

However, even if you sign this document, there is a chance that you may not be able to participate in the study (for example, if the study enrollment is complete, if you have a health condition that is not allowed in the study, etc).

The sponsor is paying for this research study. Your study doctor will be paid by the sponsor.

What is an Informed Consent?
This document is an informed consent form. It explains:

- The purpose and procedures of the study,

- Possible discomforts and risks that you may experience,
- Possible benefits that you may experience,
- Other procedures or treatments available to you (other than the procedure or treatment that is part of this study),
- How your health information will be used and disclosed in the study, and requests your permission for that use and disclosure,
- What compensation and/or medical treatment is available to you if injury occurs,
- Whom you can contact if you have any questions about the study or your rights as a research subject,
- That your participation in this study is entirely voluntary.

How does this drug work?
Fasinumab is a fully human monoclonal antibody (a type of protein) that blocks a substance called nerve growth factor (NGF). Nerve growth factor is a protein that causes pain. Blocking NGF may reduce chronic low back pain (CLBP).

This study is being done to see how effective and safe fasinumab is compared to placebo for moderate-to-severe chronic low back pain, in patients who also have OA of the hip or knee, over a 16-week treatment period. A placebo looks like the study drug, but does not contain the study drug's active ingredient(s). The term "study drug" refers to both fasinumab and placebo in this form.

How will I be given the drug?
You will have a 50% chance to be placed in fasinumab treatment group and 50% chance to be placed in fasinumab matching placebo group. You will be placed in one of the following treatment groups:

- Fasinumab 3 mg subcutaneous injection (SC) every 4 weeks
- Fasinumab-matching placebo SC every 4 weeks

The study medications will be given in a double-blinded manner. "Double-blind" means that neither you, the study doctor, nor the study staff will know who is receiving fasinumab or placebo. If needed, the study doctor will be able to find out what you are taking in case of an emergency.

The SC injections will be given in the upper arm, abdomen or thigh by the study doctor or study staff at the baseline visit, and then every 4 weeks up to Week 12. If you complete the full study treatment, you will receive a maximum of 4 injections. For the injection, a device called a pre-filled syringe will be used.

Because this is a research study, fasinumab will be given to you only during this study and not after the study is over.

What are the benefits of participating in the study?
Your participation will provide new information on the effects of this drug in patients with chronic lower back pain, which may benefit others in the future. If you receive

fasinumab and it is effective, you may experience pain relief as a result of your participation in the study, however this cannot be guaranteed.

What are the risks associated with this study?
Fasinumab may cause all, some, or none of the side effects listed below. These side effects can be mild but could also be severe or serious. There may also be unknown side effects from taking fasinumab. The risks involved in giving fasinumab are not fully known and may include possible side effects to an unborn child, if you are pregnant or become pregnant.

Risks and Possible Side Effects of Fasinumab
As of January 28, 2017, 746 people have taken fasinumab in unblinded clinical studies.

Based on a study of 419 patients with osteoarthritis of hip or knee, common side effects seen in greater than or equal to 5% (which may affect between 5 or more people in every 100) of fasinumab treated patients during the treatment period were:

- joint pain,
- headache,
- upper respiratory tract infection and
- change in feelings (such as numbness and tingling).

Joint damage occurred in patients in all dose groups, but it was more frequent at higher doses. Joint damage occurred in 1/82 (1.2%) patient in placebo, 2/85 (2.4%) in 1 mg, 4/84 (4.8%) in 3 mg, 6/85 (7.1%) in 6 mg and 10/83 (12.0%) in 9 mg fasinumab groups given every 4 weeks subcutaneously.

This joint damage usually occurred in a knee or hip and sometimes occurred in more than one joint. The joint damage often occurred with increased joint pain. For some patients, these events have resulted in joint replacement.

In large clinical studies studying monoclonal antibodies against NGF, joint damage was much more likely to occur if a group of pain medications called non-steroidal anti-inflammatory drugs or NSAIDs (such as ibuprofen) were taken together with the monoclonal antibody to NGF. However, even if you do not take non-steroidal anti-inflammatory drugs, there is a risk of joint damage with monoclonal antibodies against NGF. Since worsening of joint pain is the most common symptom of this joint damage, if you notice significantly worsening joint pain or increased joint pain that lasts more than two weeks, please notify your study doctor immediately.

From the completed and unblinded studies, joint pain and change in feelings (e.g., numbness, pins and needles, tingling) have been observed in a higher percentage of patients who received fasinumab than those who received placebo. These findings were mainly mild to moderate in severity

In animal studies, drugs that block NGF have been found to cause abnormalities in the sympathetic nervous system, the part of the nervous system that controls bodily functions such as sweating, heart rate and blood pressure. The risk in humans is unknown, and effects on the nervous system will be monitored closely during the study. If you have changes in your heart rate or blood pressure, please notify your study doctor. Examples of reasons to call your doctor include feeling light headed or dizzy. During the study, your study doctor will check for any signs of nervous system problems.

It is possible that your body may make antibodies against fasinumab. These antibodies may have the effect of causing fasinumab not to work or causing an allergic reaction. As of January 28, 2017, a few patients treated with fasinumab have developed very low amounts of antibodies against fasinumab; these antibodies have not been associated with any known side effect.

Allergic Reaction Risk
There is a chance that you will experience an allergic reaction to the study drug. Symptoms of an allergic reaction may include headache, rash, flushing, swelling, shortness of breath, nausea, or vomiting. Severe allergic reactions can cause dizziness, difficulty breathing or swallowing, a decrease in blood pressure, and could be life threatening.

In completed studies there have been no serious systemic allergic reactions reported for patients treated with fasinumab, but regardless, all administrations of fasinumab will be in the doctor's office where there is emergency equipment and medication available to treat you if needed.

As low levels of doxycycline (an antibiotic) are used in the production process of fasinumab, you may have an allergic reaction if you are allergic to doxycycline. Please, make sure to inform your study doctor or study staff if you have an allergy to doxycycline or any other medications.

A severe allergic reaction requires immediate medical treatment and could result in permanent disability or death.

If you believe you are having a severe allergic reaction, you should immediately seek emergency medical treatment, and you should alert the study doctor and study staff as soon as possible.

<u>If I stop my regular medication, what are the risks?</u>
If you stop your regular pain medication to participate in the study, your CLBP pain might get worse. Please tell the study doctor or study staff right away if you have any problems when you stop or change your regular medication.

You should tell your study doctor or a member of the study staff about any new health problems that develop while you are in this study and about any new medications you

plan to start taking (including over-the-counter medication, herbal remedies, and non-prescription drugs).

Unforeseeable Risks
It is possible that there will be other side effects associated with this study which are unknown at this time, some of which may be serious or life-threatening.

If you experience any side effects during the course of this study, you should immediately contact the study doctor.

For additional possible risks related to the clinical study procedures, see section "What do I have to do while participating in the study and what are the risks?"

How big is this study?
This study will include approximately 1020 subjects at approximately 145 centers around the world.

What are the other treatments available for my illness or condition?
There are other treatments available if you decide not to be in the study.

Alternative treatments include:

- NSAIDs such as ibuprofen (Motrin®)
- naproxen sodium (Aleve®)
- opioid drugs such as hydrocodone/acetaminophen (Vicodin®).

If you have any questions concerning alternative treatments or their risks, please ask your study doctor. You and your doctor can decide what is best for you.

How long does the study last?
Your participation in this study may last up to 64 weeks (if you have a joint replacement during the follow-up period it could be longer). You will have 10 office visits and 5 phone visits. Your participation in this study may last up to 36 weeks (if you have a joint replacement during the follow-up period it could be longer) for clinic visits. You will also have a telephone contact 52 weeks after your last dose of study drug (up to week 64).
This study has different periods. They are:

Screening

The screening period starts with the screening visit, which may be up to 30 days before your next visit. Testing (including a blood sample, a urine sample, and the taking of your vital signs including a measure of your heart rate) will be done to determine if you qualify to participate in the study. You will be examined and asked questions about your health and about your pain. You will have X rays of the shoulders, knees, and hips, and you will have an MRI(s) of several of your joints performed. You will also have a physical exam, neurological exam, and an electrocardiogram (ECG) performed.

During this screening period, you may continue to take your current pain medications for your chronic lower back pain.

Pre-Randomization Period
If you complete the screening period and meet initial eligibility criteria to continue, you will return to the site about 1 week before the baseline visit to be instructed how to use the electronic diary (eDiary) and the numeric rating scale (NRS) that will be used to rate your CLBP. You be given acetaminophen/paracetamol to take as needed for your chronic lower back pain, 2 tablets every 4 6 hours but no more than 8 tablets a day. You will also be instructed to stop medications that are not allowed during the study, including other pain medications but you will be allowed to take acetaminophen/ paracetamol as needed (according to the instructions of the study doctor). You will be instructed to report your pain levels in a daily diary along with any use of acetaminophen/paracetamol. Failure to follow these guidelines will lead to discontinuation from the study.

Double-blind Treatment period
The treatment period is 16 weeks long and will begin at the baseline visit, with visits at weeks 2, 4, 8, 12, and 16 and a phone call at week 1. You will be receiving SC injections of the study medication every 4 weeks from Baseline for a total of 4 doses (Baseline, weeks 4, 8, and 12). Your vitals will be taken before each injection. You will use the eDiary daily to report your pain score and acetaminophen/paracetamol usage.

You will be asked to complete various questionnaires such as: the daily average Low back pain intensity Numerical Rating Scale (LBPI NRS), the Roland Morris Disability Questionnaire (RMDQ), the Patient Global Assessment of Lower Back Pain (PGA of LBP), the Brief Pain Inventory-short form (BPI-sf), the Medical Outcomes Study Sleep Scale Revised (MOS Sleep-R), 36-item Short Form Survey (SF-36), the EuroQoL 5 Dimensions 5 Level Questionnaire (EQ-5D-5L), Work Productivity and Activity Impairment-Low Back Pain (WPAI-LBP), Healthcare Resource Utilization (HCRU), and the Treatment Satisfaction Questionnaire for Medication (TSQM).

You will also be asked questions about your health at each visit to monitor status of chronic low back pain. You may be required to have additional images (X-rays and MRIs) done if the study doctor thinks you need it. If you undergo a joint replacement surgery during the trial, you will be required to provide pre-op and post-op images.

Follow-up period
After the end of the treatment period (at 16 weeks after the first injection), you will continue to be monitored for an additional 20 weeks. During this follow-up period you will have two in-office visits (at 20 weeks and 36 weeks). The study staff will ask you about any side effects and your use of any medications. Other procedures performed will be neurologic and physical exams, vital signs, questionnaires regarding pain and health, blood and urine sampling, pregnancy testing, and possible x-ray/ MRIs (if deemed needed by the study doctor).

What do I have to do while participating in the study and what are the risks?If you participate, you will be asked to do the following things at different times.

Procedure Name	Possible Risks
Answer questions such as how you feel, your age, race, ethnicity, medical history food, smoking, alcohol habits, menopausal history (females only), physical activity, and previous and current medications	These questions may make you uncomfortable.
Electrocardiogram (ECG), which is an electrical measurement of your heart function.	It could hurt when they remove the electrodes which are sticky patches placed on your chest.
Vital Signs: Blood pressure, heart rate, body temperature and respiration. Blood pressure and heart rate are measured in a standing position and will be collected as part of the orthostatic hypotension assessments. Body temperature and respiration rate measurements will be collected before SC injections of the study medication.	Inflation of the blood pressure cuff may be uncomfortable. You may feel light headed when standing up from a lying position.
Blood samples for laboratory testing. Certain blood samples will require fasting (without food or drink) for 8 hours prior to being drawn.	Blood draws may cause discomfort from the needle stick, swelling, bruising at the site of the needle stick, or infection at the needle stick site. Some subjects may experience fainting or dizziness during blood draw. Fasting may cause lightheadedness or may affect blood sugar levels.
Urine samples for laboratory testing and for pregnancy testing (if you are a woman of childbearing potential).	No expected risks

Answer questions regarding your activity level, the amount of lower back and joint pain that you are experiencing, your quality of life, and possible side effects of the study medication.	These questions may make you uncomfortable.
Physical and neurological (nervous system) examination. Height and weight will also be	These may be uncomfortable.

Procedure Name	Possible Risks
taken during the study.	
X-rays will be performed to assess your OA and to determine your eligibility for the study Additional X-rays may be performed during the study if the study doctor feels that they are necessary.	X rays should not cause any discomfort; however, there is increased exposure to radiation.
MRI (magnetic resonance imaging). MRI's will be performed on the lumbar spine and may be repeated at a later time in the event of worsening of joint pain beyond your typical pain at the discretion of your study doctor.	Because an MRI can be dangerous for people with metal in their body, you must tell the study doctor whether you have metal in your body, including braces, surgical clip, pin, bullet fragment, splinter, etc, to determine if you are at risk. Otherwise, the effects of magnetic fields in an MRI scanner have been extensively studied, and there are no other known significant risks with an MRI exam. You may, however, be bothered by feelings of confinement (claustrophobia), and by the noise made by the magnet during the procedure.

Additional procedures
You will also be asked to do the following things at different times:

Starting from pre-randomization, you will be asked to record your use of rescue medication (acetaminophen/paracetamol) every day, until Week 16, in an ediary. You will also be asked to rate your pain level in the ediary every day until Week 20 as well. The study staff will provide the ediary and train you on how to record the appropriate information. The study staff can go over the training again, at any time with you, if needed.

In the event, you undergo joint (hip, knee or shoulder) replacement surgery during the study, the study medication will be stopped (if the surgery is scheduled during the study treatment period) and you will be asked to come in to the clinic for a visit before your surgery, and for two visits (at 4 weeks and 20 weeks) after the surgery during which time additional X-rays will be taken of your knees, hips, and shoulders. It is important to have the X-rays and/or MRIs before you have your joint replacement surgery.

If you experience symptoms such as “pins and needles” in your hands or feet you may be required to undergo additional tests as determined by the study doctor or a specialist. If that doctor thinks these symptoms are due to issues with your sympathetic nervous system, you may not be allowed to take any more study drug.

If you experience issues with your blood pressure that indicate a condition called orthostatic hypotension, study drug may be stopped until your symptoms go away.

While you are in the study, you must:

- Complete your ediary daily
- Follow the instructions you are given.
- Stop any prohibited medications.
- Come to the study center for all visits with the study doctor or study staff.
- Stop acetaminophen/paracetamol 24 hours prior to coming to a study visit during the treatment period.
- Maintain current physical activity and exercise levels throughout the study.
- Avoid drinking alcohol while taking paracetamol/acetaminophen.
- Fast before any scheduled blood tests as instructed by the study doctor except for the Screening (Visit 1).
- Drink 0.5 liters/16 ounces/2 cups of water before your study visits.
- Tell the study doctor or study staff about any changes in your health or the way you feel.

Tell the study doctor or study staff if you want to stop being in the study at any time.

More information about the blood tests
The maximum amount of blood taken at any single visit will be approximately 3 tablespoons (45 mL). Approximately 16 tablespoons (240 mL) will be taken from you during the entire study.

If you agree, a blood sample for DNA testing will also be taken. This is optional. You will be asked to sign a separate consent form.

The following will be tested: HbA1c (measure of long term blood glucose level), standard hematology (type and number of blood cells), blood chemistries (such as sodium, potassium, and calcium), liver panel (function of the liver), creatinine, phosphorous, and CPK (protein found in muscle), pregnancy test will be performed for women of child bearing potential.

The samples will be sent to a central laboratory for analysis. Your samples will be destroyed after all study analyses are completed.

Additional blood samples (including a blood sample for DNA testing) will be collected during the study and stored for up to 15 years following the completion of the study

The additional blood sample collection is to help Regeneron understand the following:

- How much fasinumab is present in your blood.
- How fasinumab works in the body.
- What makes some people respond better to the study drug.
- Why some people develop side effects.
- How the study drug could affect other diseases or conditions.

These additional samples will be stored in a secure storage space at Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Rd., Tarrytown, NY 10591, USA, which can be reached by email at PrecisionMedicine@regeneron.com. They will only be used for the research purposes described above. Your samples will be destroyed at the end of the storage period. If you wish to withdraw your consent to use and store your samples, please notify the study doctor in writing.

What happens if my partner or I get pregnant?

Women Who Can Get Pregnant or Are Breastfeeding:

In animal studies, fasinumab has been found to cause abnormalities in the nervous system of babies if their mothers were treated with fasinumab while pregnant.

If you are female, you must not be pregnant, nursing or become pregnant during this study because fasinumab has not yet been tested in pregnant women; unknown risks to the unborn child are possible if you become pregnant.

You must agree to use a medically acceptable method of birth control from start of study until 20 weeks after the last dose of study drug. Acceptable methods of birth control are listed below.

If you become pregnant, you may no longer participate in this study, and:

- You must tell the study doctor immediately.
- Women who become pregnant during the study will have to stop study drug
- Your study doctor will follow-up with you on the outcome of the pregnancy as required by the protocol.

As the effects of the fasinumab on a breastfed child are not known at this time, breastfeeding women cannot enroll in the study.

Acceptable methods of birth control include:

- combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, or transdermal)
- progestogen-only hormonal contraception associated with inhibition of ovulation (oral, injectable, or implantable)
- intrauterine device
- intrauterine hormone-releasing system

- bilateral tubal occlusion
- vasectomized partner 1
- sexual abstinence2

([1]Vasectomised partner is a highly effective birth control method provided that partner is the sole sexual partner of the Women of Childbearing Potential study participant and that the vasectomized partner has received medical assessment of the surgical success)

([2]Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatments. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical research study and the preferred and usual lifestyle of the subject)

Periodic abstinence, withdrawal, spermicides only, and lactational amenorrhoea method are not acceptable methods of contraception. Female condom and male condom should not be used together.

Postmenopausal women must be amenorrheic (without their periods) for at least 12 months to be considered not of childbearing potential. Pregnancy testing and contraception are not required for women with documented hysterectomy or tubal ligation.

You must notify your study doctor if you get pregnant during the study and up to 20 weeks after the last injection.

Can I change my mind about being in the study?
Taking part in this study is your choice. You may refuse to be in the study or discontinue being in the study at any time without penalty or loss of benefits. You do not need to give a reason, and your medical care and any other benefits to which you are otherwise entitled will not be affected by your decision.

If you do decide to discontinue being in the study, you should let the study doctor or the study staff know before you stop. You will be asked (if you have taken study drug) to come back to the study center for a follow-up visit at your earliest convenience. Procedures will be done to help ensure that there are no changes in your health.

If you are discontinued from the study treatment regardless the reasons you will be asked to remain in the study and complete all the remaining study visits and procedures until your study completion (without study treatment), unless you withdraw the study consent.

The information collected about you and your medical condition up to the point when you discontinue from the study, or information subsequently obtained in connection with

a safety issue related to the study, will continue to be used, including lab results, clinic notes, and any other information collected to preserve scientific validity.

What if new information becomes available?
The information in this form reflects what is known about the study at the time it is signed. If any significant new information is discovered during the study that may affect whether you want to continue to take part in the study, you will be informed in a timely manner. You may be asked to sign a new consent form if this occurs.

Why would I be asked to discontinue the study?
The study doctor or Regeneron Pharmaceuticals, Inc., the sponsor of the study ("Regeneron"), can remove you from the study without your consent at any time for any reason including:

- To improve your medical care,
- For your failure to follow the study requirements,
- If you are experiencing unusual or serious side effects,
- If you become pregnant
- If the study is stopped by the FDA or Regeneron, or
- Other reasons not itemized here.

The same procedures will be followed as those that would happen if you decided to discontinue from the study.

The sponsor or FDA may stop the study at any time.
What happens if I get injured while I am in the study?
If you think you have been injured as a result of participating in the study:

1. Promptly seek medical treatment, and
2. Call the number(s) on the first page of this form.

If you have an injury that is directly caused from the administration of fasinumab or any properly performed study procedures included in the study (procedures you receive only because of your participation in the study) and you have followed the directions of your study doctor, Regeneron will provide reimbursement for reasonable and necessary medical costs to treat your injury that are not covered by your medical or hospital insurance, or from third party or other programs providing such coverage.

Regeneron has no plans to provide monetary or financial compensation for:

a) other injury- or illness-related costs (such as lost wages, disability or discomfort due to an injury),
b) medical expenses that are paid for by a third party,
c) medical expenses that happen due to a violation of the study or other misconduct or negligence, in each case by any agent or employee of the Institution conducting the study (including the study staff), or

d) medical expenses for injury or illness unrelated to the study drug and unrelated to the proper performance of any other procedure required by the study or Regeneron's written instructions to the Institution conducting the study, including, without limitation, medical expenses associated with a pre-existing medical condition.

No funds have been set aside to provide you with any further monetary or financial compensation in case of injury.

For more information on trial related injuries, please contact the study doctor or a member of the study staff as listed on the first page of this consent.

You do not give up any legal rights by signing this consent form.

What information will the study staff look at?
Who else will be able to look at this information?
Federal regulations give you certain rights related to your health information. These include the right to know who will receive the information and how it will be used. The study doctor must obtain your authorization (permission) to use or release any health information that might identify you.

As part of this study, the study doctor and study staff ("Researchers") will collect, use and share health information about you. Except when required by law, you will not be identified by name and other personal identifying information (such as your address, date of birth, telephone number and social security number) including information they record during the research. This could include your medical history, and dates of results from physical exams, laboratory tests or other tests. In addition, your treating physicians and other healthcare providers ("Providers") may disclose health information from your medical records (from any doctor, hospital or other healthcare provider) to the Researchers. In order to not directly identify you, your initials and a code number will be used for your information.

The Researchers may use and disclose your health information to the following organizations:

- Regeneron, its collaborators in the research study or those developing the study drug, INC Research/ inVentiv Health, and their affiliates, representatives, agents, contractors and Study monitors, the Study Doctor, the Study Site and its affiliated doctors and staff (together, the "Regeneron Parties")
- The U.S. Food and Drug Administration (FDA) and other regulatory authorities in other countries
- Copernicus Group Independent Review Board (CGIRB). The IRB is a group of scientists and non-scientists who review the ethics of research. The goal of the IRB is to protect the rights and welfare of research subjects
- Other U.S. government agencies and possible government agencies of other countries

These organizations, including the Researchers, will use and disclose your health information in connection with the study to assure quality control and to analyze the health information. In addition, the Regeneron Parties may use and disclose your health information to assure the safety, effectiveness and quality of research and medical products, and as required by law, including with respect to government reporting if applicable (eg, the Centers for Medicare & Medicaid Services).

There is a risk of loss of confidentiality in research studies. Every effort will be made to protect you and your health information to the extent possible.

If you do not withdraw this Authorization, it will remain in effect.

If the research site is located in California, Delaware, Illinois, Indiana, Washington, or Wisconsin this authorization will expire on 31Dec2060.

There is no expiration of this authorization except for research conducted in the states listed above.

You have the right to review your Study Information and medical records and request changes to the Study Information if it is not correct. However, please note that during the Study, access to Study Information may be limited if it weakens the integrity of the research.

How will my information be used?
Information and results from this study may be presented at meetings or published in journals. Your name and information that can be traced back to you will not be in any presentation or publication.

Absolute confidentiality cannot be promised, because information needs to be shared. However, information will be collected and shared in accordance with applicable law. Once your health information is disclosed to the Regeneron Parties and to the other organizations identified above, it may be subject to further disclosure and no longer protected by federal privacy law. These groups are committed to keeping your health information confidential.

Will my information be on the internet?
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 if I change my mind and don't want my health information to be used?
Your decision to allow us to collect and use your health information is completely voluntary but if you do not allow us to do so, you may not participate in the study.

If you allow us to collect this information, you can change your mind at any time, and your decision will not result in any penalty or loss of benefits to which you are otherwise entitled. If you withdraw your permission, no new health information will be gathered unless you have a side effect related to the study.

You may reverse your permission to collect and use your health information at any time by sending a written notice to the study doctor at the address listed on page 1 of this form. If you reverse your permission, you will no longer be able to participate in the study.

In addition, even if you reverse your permission, your Providers, the Researchers, and the Regeneron Parties may continue to use and disclose the information they have already collected to protect the integrity of the research and as permitted by this informed consent form and authorization.

If you withdraw from the study but do not withdraw your Authorization, new health information may be collected until this study ends.

Will I have to spend money to be in this study?
There will be no cost to you for the study doctor's time or certain procedures and supplies related to this study.
The study drugs will be provided to you without charge.

You are responsible for the cost of your standard medication, in addition to any costs related to procedures and supplies not required by the study.

Will I be paid to take part?
You will not be paid for participating in this study. However, you will be reimbursed $40.00 per visit for travel to and from study visits. If you do not complete the entire study, you will be reimbursed only for the visits you traveled to while you were in the study.

What if something is developed from this research?
By participating in this study, you do not acquire any ownership rights in the samples you contribute or in any medical or genetic tests, drugs or other commercial products we may develop through this research.

If an approved product is developed from the research performed in this study, Regeneron will own all rights to the product. You will not receive money or any other form of payment for participating or from the sale of any such product.

Who do I call if I have questions?
If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, talk to the research team at the phone number(s) listed above on the first page.

This research is being overseen by an Institutional Review Board ("IRB"). You may talk to them at (888)-303-2224, irb@cgirb.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

What do I do next?
If you decide to participate in the study, you will need to read the statement below and sign and date it.

If someone explained the consent to you, they will also need to sign the consent.

SIGNATURE PAGE

Statement of the Person Signing the Consent

I have read and understand the information provided above describing the clinical trial. My questions have been satisfactorily answered and I consent to take part in this research study. I will receive a signed and dated copy of this consent form.

I authorize the release of my research and medical records and health information to the parties identified in this consent, including Regeneron, its collaborators in the study or those developing the study drug, and their affiliates, representatives agents and contractors, the Food and Drug Administration (FDA) (or other regulatory agencies) and the Institutional Review Board (IRB or IEC). By signing this consent form I have not given up any of the legal rights which I would otherwise have as a participant in a drug research study.

I voluntarily agree to take part in this research study.

Printed Name of Subject

Signature of Subject Date (DDMMMYYYY)

Statement of Person Explaining Consent

I have carefully explained to the subject the nature and purpose of the above study in language he/she understood. The subject signing this form has been given enough time and an adequate place to read and review this form. There has been an opportunity to ask questions and receive answers regarding the nature, risks, and benefits of participation in this research study. The subject appears to understand the nature and purpose of the study and the demands required of participation.

Printed Name of Person Administering Consent

Signature of Person Administering Consent Date (DDMMMYYYY)

Statement of the Witness (when applicable*)

The information in the consent form was accurately explained to, and appeared to be understood by the subject. Informed consent was freely given.

Printed Name of Impartial Witness

Signature of Impartial Witness **Date**

*Impartial Witness: If the subject cannot read, the signature of an Impartial Witness is needed.

An impartial witness is:

- a person who is independent of the trial,
- who cannot be unfairly influenced by people involved with the trial,
- who attends the informed consent process, and
- who reads the informed consent form and any other written information supplied to the subject.