UNIVERSITY OF PENNSYLVANIA

PRO140 2103, VERSION 1.0, 6 JAN 2014; LETTER OF AMENDMENT #1 28 JUL 2014, A PHASE 2A, RANDOMIZED STUDY OF PRO 140 BY SUBCUTANEOUS INJECTION IN ADULT SUBJECTS WITH HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 INFECTION

CONSENT TO PARTICIPATE IN A RESEARCH STUDY AND RESEARCH SUBJECT HIPAA AUTHORIZATION

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WHY AM I BEING ASKED TO VOLUNTEER?

You are being invited to participate in a research study because you are HIV-infected. Your participation is voluntary which means you can choose whether or not you want to participate. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the study doctor and/or the research team about this form. If you decide to participate, you will be asked to sign this form. You will get a copy to keep.

The National Institutes for Allergy and Infectious Diseases (NIAID) is providing funding for this study.

CytoDyn, Inc is providing the supply of study drug for this study.

WHY IS THIS STUDY BEING DONE?

This study is being done to better understand a new medicine designed to treat HIV infection. This study will enroll only people whose HIV does not require treatment right now. That means that if you are eligible for this trial, it is because your doctor thinks that your HIV does not need to be treated at this time. The study medication will be given over a 3-week period. There is no plan to give additional doses of the study medication beyond this time frame. That means even if the study drug works to decrease the amount of HIV virus in your body, that effect will almost certainly be temporary. It is unlikely that you will have any long term benefit to your HIV from being in this study. However, the knowledge gained from this study may lead to new treatment options for HIV in the future.

PRO 140 belongs to the monoclonal antibody class of medicines. Monoclonal antibodies are synthetic versions of the disease-fighting proteins (antibodies) that are naturally produced by the body.

Antibodies that are normally present in the blood typically react to foreign organisms or materials (bacteria, viruses, etc.). However, PRO 140 binds to a protein (CCR5) that is found on certain human immune cells (blood cells that fight infections). They are the pathways by which the HIV-1 virus infects the cell. When PRO 140 binds to the CCR5 receptor on these immune cells, HIV cannot attach itself to the cell, and cannot infect the cell.

This study is being conducted to determine:

- The safety (how well your body tolerates the study drug and what side effects you may experience) and effectiveness (how well it works) of PRO 140
- The effectiveness of PRO 140 at interfering with HIV in the body
- The effectiveness of the treatment doses of PRO 140 that you will receive compared to other treatment doses of PRO 140.
- If HIV becomes resistant to PRO 140 and , if so, how does it become resistant
- How much and for how long PRO 140 stays in the blood
- What, if any, are the responses of your immune system to PRO 140
- To identify doses of PRO 140 for future studies.

The safety and effectiveness of PRO 140 has been previously evaluated in 100 people in previous studies, 84 of whom were infected with the HIV virus and have characteristics similar to you. Previous studies of PRO 140 given by injection under the skin and by injection into the blood in persons infected with HIV found PRO 140 to be safe and be active at interfering with HIV. Mathematical estimations based on these studies have been used to guide the choices of treatment doses of PRO 140 to be used in this study. The 700mg dose of PRO 140 has not been administered by injection under the skin to persons before, but the comparable dose has been given by injection into the blood safely and with anti-HIV effect to HIV-infected persons before. This particular formation of PRO 140 (what PRO 140 is mixed in) has been given safely to 14 people not infected with HIV, but not yet to people infected with HIV. The product you will be using is an investigational drug. An investigational drug is one that is under study but not yet approved by the U.S. Food and Drug Administration (FDA). It is currently not available outside of clinical trials. The results of these studies will be used to design future studies that may result in the approval of this drug for the treatment of HIV-1 infection.

In order to take part in this study, you must be willing to:

- allow the physician to administer study drug subcutaneously. This means the drug will be administered in a syringe and very thin needle slightly below the surface of your skin in either your arm, abdomen or thigh
- show up for all visits on time
- allow a total of approximately 31 tablespoons of blood to be collected throughout the study
- allow some of your blood to be stored for extra testing

If you decide to take part in this study, you will be screened to determine if you meet the requirements of the study. If you qualify for this research study, you will be asked to return to the clinic for 11 additional scheduled visits as a participant in the study. You will be randomly assigned to one of four treatment groups (like the flip of the coin). In each of the treatment groups, you will receive PRO 140 but the doses of PRO 140 and when they will be administered will depend on which treatment group you're assigned to. Study drug will be administered either through the surface of your arm, thigh or stomach. You will not be able to receive additional doses of the study drug after

your last dose.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 40 people will take part in this study across all sites in the U.S.. At the University of Pennsylvania about 5-7 people are expected to participate.

WHAT DO I HAVE TO DO IF I AM IN THIS STUDY?

Screening Visit1

There will be two screening visits over approximately a 12-week period. At the first screening visit, the following will be done:

- Confirmation of your HIV-1 diagnosis. If written documentation of the diagnosis is not available, a test will be done which requires approximately one half tablespoon of blood to be drawn.
- A blood test to determine whether the HIV-1 virus in your body binds to the CCR5 receptor protein or also uses another protein, CXCR4. Early in the course of infection, most HIV-1 binds to immune cells by only using CCR5, but a small percentage use CXCR4. Only subjects with HIV-1 that bind to CCR5 alone will be eligible for the study. In order to perform this test, approximately one and one half tablespoons of blood will be taken.
- Answer questions about your background, medical history, current health, and any medication you may have taken, and any associated side effects. This is necessary because some medications and/or aspects of your medical history may disqualify you from participation in the study.

This visit may take up to two hours. If, at the end of this visit, you have satisfied all the criteria necessary to move to the next stage of evaluation, you will be asked to return for a second screening visit up to nine weeks later (up to three weeks before receiving the study product). The waiting time between the two visits is because some of the laboratory tests require time for processing.

Screening Visit2

This second screening visit may take two to three hours. At this second screening visit, the following will be done:

- Physical examination and vital signs
- ECG (electrocardiogram – a test to check your heart)
- Blood samples drawn (approximately 2.0 tablespoons of blood) for general health, as well as to determine the amount of virus you have
- Answer questions about your medical history, current health, any medication you may have taken in the past or are currently taking and any side effects you may have experienced from these medications
- serum pregnancy test for women
- Rectal Biopsy- this is an optional procedure. It will take place anytime between the second screening visit and just prior to Day 1. If you decide to participate, several small samples of the skin lining the inside your rectum will be taken. The lining regrows within a day or so. The procedure will take approximately 30 minutes to complete and is performed in the outpatient clinic. The biopsy does not usually require pain medications. You must refrain from anal sex or insertion of any object in the rectum for three (3) weeks after each rectal

biopsy procedure. Based on your medical history, your study doctor may determine that you need to take antibiotics for a few days before the procedure, if you have another condition that requires antibiotics at the time of the procedure. This biopsy is optional, which means that you can refuse to have the procedure done. Your choice will not affect whether or not you can participate in the study.

Even if you have passed all the screening requirements, you may not receive study drug if a medical condition develops prior to receiving study drug that, in the opinion of the study doctor, could be a possible safety issue for you if you participated in the study. This includes but is not limited to unexplained temperature (>38.5 degrees Celsius or 101.3 degrees Fahrenheit) for seven days in a row within two weeks before you receive the study drug.

Entry Visit (Treatment Visit-Day1)

If you qualify for this research study, you will be asked to return to the clinic for 11 additional scheduled visits as a participant in the study. You will be randomly assigned to one of four treatment groups (like the flip of the coin). In each of the treatment groups, you will receive PRO 140 but the doses of PRO140 and when they will be administered will depend on which treatment group you are assigned. Study drug will be administered either through the surface of your arm, thigh or stomach. You will not be able to receive additional doses of the study drug after your last dose.

Depending on which treatment group you are in, you may receive three doses of study drug throughout the study.

At the treatment visit (Day 1), the following will be done:

- Urine pregnancy test in women, Study drug will not be administered if urine pregnancy test is positive.
- Injection of the study drug using a device known as an Autoject®2 pen. The pen is a spring loaded semi-automatic device that rapidly injects the drug into your subcutaneous tissue. There will be four injections on Day 1 either on the surface of your arm, thigh or stomach depending on which treatment group you are put into. This method of drug administration has been used by many patients before and produces only a mild sting in the great majority of individuals
- Physical examination and vital signs (including weight assessment)
- ECG
- Blood samples (approximately 3.0 tablespoons of blood) will be drawn at various time points throughout the day to assess your general health, to determine the type virus you have, and to determine the amount of study drug and how the drug influences the amount of virus you have. These samples may be taken through a hep-lock (a device that is inserted through the skin that prevents the blood from clotting at that site and allows for blood to be drawn through a needle) or through multiple needle sticks.
- You will be asked about your health and any medication you may have taken, and any side effects you may have experienced

This visit may take 7 hours in total to complete. This includes approximately six hours of follow-up procedures once the injection is completed.

On Study Treatment Visit (Days 2, 3, 5, 8, 10, 15, 17, 22, 29, and 59)

You will be asked to return for all follow-up visits on Days 2, 3, 5, 8, 10, 15, 17, 22, 29, and 59.

The following tests will be performed on the days indicated:

- Vital signs (Days 2, 3, 5, 10, 17, 22, and 29)
- ECG (Days 3, 10, and 22)
- Physical examination (Day 22)
- Blood samples will be drawn to determine the type and amount of virus you have, the amount of study drug you have and how the drug influences the amount of virus you have and to measure your general health (Days 2, 3, 5, 10, 17, 22, and 29). In total, approximately 9.5 tablespoons of blood will be drawn during these visits (approximately 0.5 tablespoons on Days 2, 5 and 10, approximately 1.5 tablespoons on Days 3 and 17, and approximately 2.5 tablespoons on Days 22 and 29)
- Rectal biopsy procedure (optional; Day 15 rectal biopsy is only required if you are in treatment group 4. Day 29 rectal biopsy procedures will be performed if you're in treatment groups 1-3)
- You will be asked about your health and any medication you may have taken, and any side effects you may have experienced (Days 2, 3, 5, 10, 17, 22, and 29)

On Study Treatment Visit (Days 8 and 15)

At treatment visits (Days 8 and 15), the following will be done:

- Urine pregnancy test in women, Study drug will not be administered if urine pregnancy test is positive.
- Injection of the study drug using a device known as an Autoject®2 pen either through the surface of your arm, thigh stomach depending on which treatment group you are put into. For these visits, only two injections will be administered.
- Physical examination and vital signs
- ECG (Day 8 only)
- Blood samples (approximately 2.5 tablespoons on Day 8 and approximately 3.0 tablespoons on Day 15) will be drawn to assess your general health, to determine the type and amount of virus you have, and to determine the amount of study drug and how the drug influences the amount of virus you have
- You will be asked about your health and any medication you may have taken, and any side effects you may have experienced
- You will be asked to complete questionnaires related to your well-being and experience with self-administration of study drug (day 15 only).

Your last visit (Day 59 or the last day you are enrolled in the study) is a close out visit and the following will be done:

- Physical examination and vital signs (including weight assessment)
  Blood samples (approximately 3.0 tablespoons of blood) may be drawn for general health, to determine the type and amount of virus you have, and to determine what the study product is doing in your body
- ECG
- You will be asked about your health and any medication you may have taken, and any side effects you may have experienced
- Urine pregnancy test

You will be asked to complete this visit even if you discontinue the study before Day 59. This is important to understand how you and your body responded to the study drug during the study. In the unlikely event that, at your last visit, your virus levels (viral load) continue to be lower than baseline, you may be asked to return for more visits where more blood samples will be drawn (approximately 1 teaspoon).

Medically relevant results may be provided to you during the course of this study upon request. However, certain test results will only be made available upon completion of the study. Other test results specifically related to PRO 140 will not be provided to individual subjects.

Blood specimens will be retained after the study for future research and will be stored at Drexel University for 10 years. Research staff in the Division of Infectious Diseases and HIV Medicine and potential future research collaborators will have access to these specimens.

HOW LONG WILL I BE IN THIS STUDY?

You will receive three doses of the study drug (Days 1, 8 and 15). After the two screening visits are complete, you will be on study for approximately 2 months (59 days).

WHY WOULD THE DOCTOR TAKE ME OFF THIS STUDY EARLY?

You may be required to stop your participation before the end of the study for any of the following reasons:

a) A change in your medical condition;
b) Your viral load increases after being low (you will not be able to receive study treatment but you will continue to attend study visit until the study ends)
c) You need to start taking medications to treat your HIV (you will not be able to receive study treatment but you will continue to attend study visit until the study ends)
d) You become pregnant (you will not be able to receive study treatment but you will continue to attend study visit until the study ends)
e) Regulatory agencies decide to stop study drug treatment
f) Discontinuation of all or part of the study; or
g) Other reasons, including new information available to the investigator or harmful reasons experienced by you or other subjects in this study.

If you leave the study before the final regularly scheduled visit, the study doctor may ask you to make a final visit for some of the end of study procedures.

WHAT ARE THE RISKS OF THE STUDY DRUG (PRO-140)?

- It is possible that the study drug will not help your HIV-1 infection and it may even get worse during the study. The most common study drug-related side effect that has been seen using the drug formulation is mild headache. This side effect occurs occasionally. Other less common side effects likely to be related to the drug include mild to moderate diarrhea, nausea, and fatigue.

- PRO 140 belongs to the monoclonal antibody class of drugs. Monoclonal antibodies are sometimes associated with allergic reactions which may include the following: fatigue, diarrhea, fever, vomiting, headache, nausea, pain at the site of infusion, low blood pressure, rash, itching, and chills or flu-like reactions such as fever, chills, and aches. These events are uncommon and are usually of short duration if they occur at all.

- It is possible you may have an allergic reaction, which can sometimes be life threatening.

- People who take PRO 140 or other monoclonal antibodies can also develop an immune response to PRO 140 that may affect their ability to receive monoclonal antibodies, or to benefit from diagnosis or therapy with a monoclonal antibody in the future. This is an uncommon risk.

- Side effects that may be associated within a short period of time after receiving drugs like PRO 140 through an infusion include chills, headache, backache, overall feeling of being ill, fever, skin rash, nausea, tingling and high blood pressure. These side effects are uncommon and your study doctor may give you medicine to help with these side effects.

- Local pain, redness, tenderness, bruising, itching are occasional side effects of receiving the injections; rarely, an infection might occur at the site of the needle stick or you may faint when blood is collected.

- The may be risks associated with the rectal biopsy procedure. These may include mild rectal irritation/urgency and rectal bleeding (limited) for 2-3 days post-procedure. There is the possibility of extremely rare complications, such as infection or bowel perforations. Should these occur, antibiotics or surgical repair may be required. You should refrain from receiving anal intercourse for 5 days after the procedure. You will be monitored for any complications. Prophylactic antibiotics will be given to any subject who would routinely be given such treatment prior to invasive procedures.

- Studies on PRO 140 to determine its capability to cause harm to an unborn child have not been performed. Therefore, if you are pregnant or think you might be, you will not be allowed to participate in this study. If you are a woman of childbearing potential, you will be tested for pregnancy at the beginning and end of the study, and are asked to use consistent birth control throughout the study. If you become pregnant during the study, you will not be allowed to continuing receiving PRO 140. You will, however, continue to attend study visits until the study ends. If your pregnancy is not completed at the final study visit, we may contact you through monthly phone calls to determine the outcome.

- It is unknown if PRO 140 can pass through breast milk and it is unknown if this can cause harm to your child.
- It is possible that your HIV may use the other co-receptor (where the virus attaches), CXCR4, to enter and infect cells in addition to the CCR5 use detected when you screened for the study and it was not detected by the test, or that such a virus may emerge during treatment with PRO 140. In either case, your HIV virus may not respond as well to treatment with PRO 140. If a CXCR4-using HIV emerged or was unmasked during treatment, this virus has been associated with a faster course of disease progression and is not treatable with maraviroc,

one anti-HIV medicine that also binds to the CCR5 co-receptor. However, it will still be treatable t with all other anti-HIV medicines to which it was treatable before your participation in this study.

- During this study (59 days), you will not be able to receive any other anti-retroviral therapy for your HIV-1 infection. This should be discussed with your doctor. Current HIV treatment guidelines recommend that all patients with HIV be treated with anti-HIV medicines to avoid the complications of HIV infection. You will be permitted to start anti-HIV medicines at any time that your doctor feels it is in your best interest. Your doctor might recommend you start these medications if your CD4 count drops below 350 cells/mm^3. If you start anti-HIV medicines, you will not be able to receive additional doses of PRO 140 but will be encouraged to complete all study visits and procedures.

- Individuals who lack a functional CCR5 gene may be at increased risk for severe infection by West Nile virus Because of this, treatment with anti-CCR5 drugs poses a theoretical risk for increased severity of West Nile virus infection. This has not been established to be a risk with maraviroc, the anti-CCR5 drug already FDA-approved for the treatment of HIV and therefore would not be expected to be a problem with this antibody

There may be side effects which are unknown at this time. Unexpected reactions, hazards, discomforts and inconveniences may affect the quality of life and may include life-threatening events or death.

Your disease may not get better or may become worse while you are in this study.

ARE THERE RISKS RELATED TO PREGNANCY?

You should not become pregnant while on this research study. You must use effective birth control throughout the course of this study and for 3 months after that. You must agree not to attempt to become pregnant or to impregnate and you must agree to use one barrier method of birth control plus one other highly reliable contraceptive method (e.g., condom with spermicide plus diaphragm) throughout the course of this study and for three weeks after receiving your last dose of PRO 140. If you or your partner becomes pregnant while in the study, you must tell the study doctor as soon as possible.

If you are or become pregnant, this research may hurt your baby or your pregnancy in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death.

The Antiretrovial Pregnancy Registry (http://www.apregistry.com) enrolls subjects, (through their health care provider) who become pregnant while on study. Pregnant subjects may learn about the Registry or other related information or sites by following the "Patients" link at the Registry site.

If you are a woman, you must have a negative pregnancy test at your second screening visit. If you become pregnant during the course of this study, you will be followed until 3 months after the birth of the child. This will consist of telephone contact to determine the end result of the pregnancy and whether there were any side effects on the fetus/infant .

You and your insurance company will be charged for the health care services that you would ordinarily be responsible to pay. In some cases, insurance will not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay.

ARE THERE BENEFITS TO TAKING PART IN THIS STUDY?

The short duration of study treatment means that there is very little chance that your HIV disease will improve because of this treatment. If you are in one of the 3 groups receiving active medication, your viral load may decrease temporarily and your CD4 count may increase temporarily, but it is unlikely that these short term changes will have any long term benefit to you. It is possible that you may benefit from the monitoring of your HIV as a participant in this study. There may be no direct benefits to you from participating in this study.

The knowledge obtained from this research may help the health care professionals caring for you to better understand your condition and how to treat it.

WHAT OTHER CHOICES DO I HAVE BESIDES THIS STUDY?

The alternative is not to participate in this study. Your doctor has discussed the other options available to you including other types of HIV-1 treatment or no treatment at all at the present time. You and your doctor can make the best choice of alternate treatment. If you decide not to take part in this study, it will not affect your future treatment. You do not have to participate in this study to be treated for your HIV disease

WHAT ABOUT CONFIDENTIALITY?

By signing this Consent/Authorization Form you are permitting the University of Pennsylvania Health System and the School of Medicine to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania Health System and the School of Medicine to disclose that personal health information to outside organizations or people involved with the processing of this study.

<u>What personal health information is collected and used in this study, and also might be shared?</u>

The following personal health information will be collected, used for research, and may be disclosed during your involvement with this research study:

- Name, address, telephone number, email address
- Dates directly related to you such as date of birth and clinic visits.
- Personal and family medical history
- Current and past medications or therapies
- Questionnaires
- Results of tests and procedures you will undergo during this research
- Social Security Number, Medical record number

Why is your personal health information being used?

Personal contact information, such as phone number and address, will be used only by clinical trial staff to get in touch with you while you are participating in this study. Your health information and results of tests and procedures are being collected as part of the research study and for the advancement of medicine and clinical care. The Principal Investigator will use the results to monitor your safety and ability to tolerate the study medications.

Which of our personnel may use or disclose your personal health information?

The following individuals and organizations may use or disclose your personal health information for this research project:

- The Principal Investigator and other University staff associated with this study;
- The University of Pennsylvania Institutional Review Boards (the Committees charged with overseeing research on human subjects) and the University of Pennsylvania Office of Regulatory Affairs
- Authorized members of the University of Pennsylvania and the University of Pennsylvania Health System and School of Medicine work force who may need to access your information in the performance of their duties, for example, to provide treatment, to ensure the integrity of the research, accounting or billing matters, etc.

Who, outside of the University of Pennsylvania Health System and the School of Medicine, might receive your personal health information?

As part of the study the Principal Investigator, study team and others listed above, may disclose your personal health information, including the results of the research study tests and procedures to the following:

- Pharmaceutical Sponsors: Drug companies (CytoDyn, Inc) who supply treatment for the study will have access to safety information.
- Data Coordinating Center, Frontier Science Technology Research Foundation (FSTRF): Data for this study will be recorded on case report forms, keyed into a central database and electronically submitted to the Data Coordinating Center. The data will be stored at this facility until it is ready to be analyzed.
- Contract Research Organization (PPD, Inc): Monitors from PPD will visit the site on a regularly basis to review data and correct mistakes before the data are analyzed.
- Study Sponsor: Drexel College of Medicine, the coordinating center for the study, will have access to safety information.
- Government Agencies: Data from this study will be made available to the Food and Drug Administration and the National Institutes of Health (NIH), for them to evaluate the safety and efficacy of the treatments being used in this study.

Study staff will inform you if there are any changes to this list above during your active participation in the trial. Once information is disclosed to others outside the University of Pennsylvania Health System or School of Medicine the information may no longer be covered by federal privacy protection regulations.

In all disclosures outside the University of Pennsylvania Health System or School of Medicine, 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. Personal health

information will be disclosed by a unique code number. Only study staff can break the code and identify you to your code.

How long will the University of Pennsylvania Health System and the School of Medicine be able to use or disclose your personal health information?

Your authorization for use of your personal information for this specific study does not expire. This information may be stored in a database (research repository). However, the University of Pennsylvania Health System and the School of Medicine may not re-use or re-disclose your personal health information collected for this study for another purpose other than the research described in this consent form unless you have given written permission to the Principal Investigator to do so. However, the University of Pennsylvania Institutional Review Board may grant permission to the Principal Investigator or others to use your information for another purpose after ensuring that appropriate safeguards are in place. The Institutional Review Board is a committee whose job is to protect the safety and privacy of research subjects. Results of all tests and procedures done solely for this research study and not as part of your regular care will not be included in your medical record unless you want them to be sent to your primary care provider. You will need to complete a medical records release of information to allow us to provide study data to your doctor.

Will you be able to access your records?

You will be able to request access to your medical record when the study is completed. During your participation in the study, you will not be able to access your medical records. This will be done to prevent the knowledge of study results affecting the reliability of the study. Your information will be available should an emergency arise that would require your treating physician to know the information to best treat you. You will have access to your medical record and study information that is part of that record when the study is over. The Investigator is not required to release to you research information that is not part of your medical record.

Can you change your mind?

You may withdraw your permission for the use and disclosure of any of your personal information for research, but you must do so in writing to the Principal Investigator at 502 Johnson Pavilion. Even if you withdraw your permission, the Principal Investigator for the research study may still use your personal information that was collected prior to your written request if that information is necessary to the study. If you withdraw your permission to use your personal health information that means you will also be withdrawn from the research study.

WWW. CLINICALTRIALS.GOV

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 an Electronic Medical Record?

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, results of research-related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS.

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you for the purpose of maintaining any results of procedures performed as part of this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Results of research procedures performed as part of your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.

Once placed in your EMR, these results are accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc).

WHAT ARE THE COSTS TO ME?
The study drug (PRO-140), exams, and blood tests will be provided for free.

You will not be charged for any tests specifically required for this research study, but you or your insurance company will still be billed for tests or procedures that are considered "standard of care" and would have been part of your medical treatment even if you did not participate in this study. These treatment costs include but are not limited to drugs, routine laboratory tests, x-rays, scans, surgeries, routine medical care, and physician charges. Your health insurance company may not pay for these "standard of care" charges because you are in a research study. If your insurance company does not pay for costs associated with this research study that are considered "standard of care" for your medical treatment, then you will be billed for these costs. You are responsible for paying for any insurance co-pays and any deductibles due under your insurance policy, and any charges your insurance company does not pay.

WILL I RECEIVE ANY PAYMENT?
Yes. You will be compensated $25 for each of the Screening visits; $100 for the Enroll visit (a 7 hr PK visit); and $50 for the 10 scheduled on-study visits. Thus, if you attend all visits, the maximum compensation you can receive is $650. Participants are not compensated for visits not attended. Participants who elect to have rectal biopsies will receive $100 for each biopsy (2). Compensation for these visits will be given as a check after the visit is completed.

Please note that if you receive more than $600.00 compensation in one year for participation in research studies at the University of Pennsylvania, you must provide a Individual Tax Identification number or Social Security Number for tax purposes.

WHAT HAPPENS IF I AM INJURED?
If you have a medical emergency during the study you may contact the Principal Investigator or Emergency contact listed on page one of this form. You may also contact your own doctor, or seek treatment outside of the University of Pennsylvania. Be sure to tell the doctor or his/her staff that

you are in a research study being conducted at the University of Pennsylvania. Ask them to call the telephone numbers on the first page of this consent form for further instructions or information about your care.

In the event of any physical injury resulting from research procedures, medical treatment will be provided without cost to you, but financial compensation is not otherwise available from the University of Pennsylvania. If you have an illness or injury during this research trial that is not directly related to your participation in this study, you and/or your insurance will be responsible for the cost of the medical care of that illness or injury.

WILL I BE TOLD ABOUT NEW INFORMATION?

We will tell you about new information from this or other studies that may affect your health, welfare, or willingness to stay in this study. If you would like the results of the study, let the study staff know.

WHAT DO I DO IF I HAVE QUESTIONS OR PROBLEMS?

For questions about this study or a research-related injury, contact:

- Pablo Tebas, MD (215-349-8092)
- Clinical Trials Unit (215 349-8092)

For questions about your rights as a research subject, contact:

- Director of Regulatory Affairs at the University of Pennsylvania by phoning (215) 898-2614

SIGNATURE PAGE FOR STUDY

If you have read this consent form (or had it explained to you), all your questions have been answered and you agree to take part in this study, please sign your name below.

_____	_____
Participant's Name (print)	Participant's Signature and Date
_____	_____
Study Staff Conducting Consent Discussion (print)	Study Staff Signature and Date