CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY

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Important new information has been discovered during this clinical trial that may have an impact on your continued consent to participate in this clinical trial.

OBSERVATIONAL COMPONENT
As a current participant in the active phase of the A4001027 protocol you are being asked to discontinue from the active phase and to participate in the long term observational phase of the study. As a participant you currently come in for study visits once every twelve weeks. In the observational phase you will be required to come in for study visits every 6 months. During these visits your health status will be evaluated and if you are currently receiving study drug, you will be provided with a re-supply of medication. If you are not currently receiving study drug your health status evaluation may be done by telephone. No laboratory tests or study procedures will be required.

If you previously participated in the A4001027 study you are being asked to re-enter the study and participate in the long term observational phase. When you re-enter the study, you will be contacted by your study team by telephone and asked a series of questions to evaluate your state of health. After this first evaluation, you will be contacted every six months and asked the same series of questions. No clinic or hospital visits will be required.

Your participation may last up to 5 years from the time of your first dose of study treatment. You will be asked to provide a secondary contact (i.e. next of kin) and your primary care physician (if it applies to you) in the event that your study team is not able to reach you for your 6 month visit or telephone call. This contact information will be documented in your medical record. In the event that your study team is unable to contact you, your secondary contact, or your primary care physician; then the death registry may be searched. You will remain anonymous to the sponsor throughout this observational phase of the study.

NATURE AND PURPOSE OF STUDY
You are being asked to take part in a research drug study run by Pfizer Inc. You are being asked to take part because you may have a specific type of HIV called CCR5-tropic virus. Pfizer, Inc. is doing this research study to look at the good and bad effects of an investigational new drug named UK-427,857 that may help people with HIV. The drug UK-427,857 is in a new class of antiretroviral agents called entry inhibitors (blocks HIV from entering cells). Thus far, it has been given to about 501 healthy and 66 HIV infected volunteers in other studies. In most patients, untreated infection with HIV leads to progressive disease, AIDS, and death.
HIV causes disease by preventing the immune system (the body’s defense against infections) from working properly. HIV is able to infect and destroy cells of the immune system (CD4 cells) and to stop
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them from working. The virus destroys many of the CD4 cells. If you remain untreated, it is likely that your CD4 count (number of CD4 cells in the blood) will go down and the amount of HIV in the blood stream (viral load) will go up. This will lead to a faster disease progression. The aim of this research is to keep the amount of HIV as low as possible. When HIV decreases in the blood stream because of drug treatment, the number of CD4 cells generally increases. In most patients, the use of different drug combinations to control the disease has had a significant impact on patient survival, however failure of therapy due to drug resistance and/or lack of toleration is a significant problem. The development of new drugs to treat HIV infection, therefore, remains important.

In order for HIV to cause infection in new cells, it needs to get into the cells where it can produce new HIV. To do this, HIV attaches itself to the cell via a receptor on the cell surface. This is similar to two people shaking hands. HIV uses a combination of the CD4 receptor and another co-receptor (CCR5 or CXCR4) to attach to the cell. In this “handshake” between HIV and the cell, the virus is able to enter into the cell.

In the early stages of disease HIV uses the CCR5 receptor 80-90% of the time. This type of virus is called CCR5 tropic or R5 virus. In later disease stages, approximately 50% of patients are infected with virus that enters cells by using the CXCR4 receptor. Virus that uses the CXCR4 receptor is called CXCR4 tropic or X4 virus. If this change happens, it normally occurs when there is a rapid fall in CD4 cells. However, it is not clear whether this change is directly responsible for the rapid CD4 cell loss, as 50% of patients experience CD4 cell loss and disease progression without developing HIV that uses the CXCR4 receptor.

There have been studies of people who have been exposed to HIV, but did not become infected. Many of these people have a different form of the CCR5 gene (called delta 32) resulting in a high level of protection from HIV infection. Those people with two copies of the CCR5 delta 32 gene have the most protection. People with one copy of CCR5 delta 32 are not protected from becoming infected with HIV, but if they become HIV infected, they may take longer to become ill and develop AIDS.

Based on the data above, it is likely that blocking the CCR5 receptor will prevent HIV from multiplying and spreading further in the cells of the body. UK-427,857 acts by preventing the virus from binding to the CCR5 receptor. In two studies, 66 CCR5 tropic HIV-1 infected patients received UK-427,857. HIV was decreased by approximately 10-40 fold at doses that will be used in this trial.

Optimized Background Therapy (OBT) is determined by your study physician and consists of the best combination of current drugs available to treat your HIV based on testing of your virus for resistance to the various antiretroviral drugs. You will be responsible for obtaining and paying for your OBT. You will receive either UK-427,857 or placebo in addition to your OBT. UK-427,857 and/or placebo will be in tablet form and dosing will occur twice a day. Placebo is a pill that does not contain any drug. You have an 80% (4 out of 5) chance of getting UK-427,857, in addition to OBT, as part of your dosing regimen (either 150mg once a day or 150mg twice daily). This means 20% (1 out of 5) people will receive a placebo/dummy drug in addition to the optimized background therapy. Because this is a double blind study, neither you nor your doctor will know which drug you are receiving, although in an emergency, this information is available.
The purpose of this study is:

- To determine if UK-427,857 when added to OBT will cause a decrease in HIV-1 RNA (viral load) that is greater than OBT alone.
- To determine if UK-427,857 is safe and well tolerated in HIV-infected people when added to OBT versus OBT alone.

Because this is a research study, UK-427,857 will be provided by the sponsor (unless the sponsor discontinues development of UK-427,857) during this study and until it is commercially available if you complete 48 weeks of therapy and it is determined that you will continue to benefit with UK-427,857 therapy. Patients will continue on blinded therapy in the study until the last patient enrolled in the study reaches their Week 48 visit. Then follow up visits will be scheduled for another year after that at a minimum. The visit schedule for the period beyond the week 48 visit will be every 12 weeks.

During the course of any research project, new information may be available about the drugs being studied. If this happens, your doctor will tell you about it and discuss whether you want to continue taking part in the study. In the unlikely event that the sponsor discontinues a treatment group from the study, the study doctor will discuss treatment options with those subjects that are affected by the change. Treatment options may include switching to an alternative on-study treatment group and be monitored or be discontinued from the study. If you decide to withdraw, your study doctor will make arrangements for your care to continue. If you decide to continue you will be asked to sign an updated consent form.

If you exit the study you will need to complete all the tests required at the early termination visit. Your doctor will discuss alternative treatments for you and you will be monitored in the study on your new regimen.

**PROCEDURES**

**STUDY VISIT SCHEDULE**

You may transition to the observational phase at either your regular scheduled visit (every 3 months) or at an unplanned visit.

**STUDY EVALUATIONS AND TREATMENT**

During the study you will be seen as an outpatient. You will be asked to attend the clinic for up to 48 weeks after beginning study drug. Appointments will include a screening visit, a randomization visit, Day 1 (Baseline) visit when study drug therapy will begin, along with follow-up visits scheduled at 2, 4, 8, 12, 16, 20, 24, 32, 40, and 48 weeks. Please refer to the study visit plan at the back of this document.

The first visit (screening visit) will help to determine if you can be accepted into the full study and will include: a sample of your blood for testing in the laboratory. The blood analysis includes chemistry, hematology, hepatitis B and C, HIV, CD4 and CD8 cell count, viral load, viral tropism (to determine whether your virus uses CCR5, CXCR4 or both to enter the cell), viral resistance, and a pregnancy test for women of child bearing potential.

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Approximately 4-5 weeks from the screening visit you will be asked to return for a randomization visit. The results from the screening visit will be reviewed and the clinic doctor will determine if you can be accepted into the study. You will be eligible for the treatment only if you have CCR5 tropic virus. At this time, the doctor will decide what OBT would be best for you based on the results of your screening tests. In addition, a sample of your blood to measure viral load will be taken if you are accepted. If your HIV is not a CCR5 tropic virus or cannot be determined by the co-receptor tropism assay, you may be offered enrollment in a related study A4001029. This study will require a new A4001029 consent form and transfer of your current screening tests.

After the randomization visit, you will return to the clinic within 7 days to begin the treatment phase of the trial (baseline visit). At this time, you will have a complete physical examination; a sample of your blood and urine will be taken for testing (refer to the study visit plan), as well as a measurement of your blood pressure and pulse rate and a painless recording of the activity of your heart called an electrocardiogram (ECG). You will also be given study medication.

**DOsing schedule**

Once accepted, you will be randomly assigned to one of 3 possible treatment groups:
- OBT (3-6 drugs based on treatment history and resistance testing) + UK427,857 150mg by mouth once daily
- OBT (3-6 drugs based on treatment history and resistance testing) + UK427,857 150mg by mouth twice daily
- OBT (3-6 drugs based on treatment history and resistance testing) + placebo by mouth twice daily

UK-427,857 and/or placebo will be in tablet form. Dosing will occur twice a day. It is very important to take your medication (both OBT and study medication) exactly as prescribed. You will be informed how many tablets to take from the morning and evening bottles (12 hours between doses). Neither you nor your doctor will know which drug you are receiving, although in an emergency, this information is available.

**Visits following Baseline to Week 48:**

During the visits (see visit plan) samples of your blood (approximately 50 ml or 3-4 tablespoons) will be taken via a needle inserted into a vein in your arm. Ongoing tests will include:
- UK-427,857 in your blood
- Viral load (amount of HIV particles in the blood plasma)
- Viral tropism (whether your virus uses CCR5 to enter the cell, i.e. is the right type of virus for treatment with UK-427,857)
- Numbers of CD4 and CD8 cells
- Sensitivity of your virus to UK-427,857 (i.e. how much UK-427,857 is needed to stop the virus from multiplying). An additional blood sample will be used by Pfizer to grow the virus (virus isolation) and test its sensitivity to UK-427,857 if required. These samples may also be used to evaluate the anti-HIV activity of other Pfizer anti-retroviral drugs in pre-clinical and clinical development. Other susceptibility and/or tropism tests may be performed on these samples.
- Pregnancy: All female patients of childbearing potential will be tested throughout the study, using either a blood or urine sample, to ensure they are not pregnant.
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Follow-up Visits After Week 48 to End of Study:
- Targeted physical examination and vital signs.
- Assessment of signs, symptoms and adverse events
- Review of concomitant medications
- Serum chemistry and hematology
- Hepatitis C virus RNA if you were Hepatitis C antibody positive at screening
- CD4 and CD8 lymphocyte determinations (absolute and percent);
- Plasma HIV-1 RNA level as determined by the Roche Amplicor HIV-1 MONITOR tests, standard method (if the results of the standard method are <400 copies/ml, the ultrasensitive method will automatically be performed)
- Blood sampling for preparation of two 1 ml plasma aliquots (frozen) stored for future testing
- Urine Pregnancy test for Women of Childbearing potential. A positive urine test will require a confirmatory serum pregnancy test.
- Plasma sample for HIV-1 co-receptor tropism phenotype as determined by the Monogram Biologics recombinant virus entry assay upon treatment failure as defined in the protocol, (this sample is to be drawn when the confirmatory plasma HIV-1 RNA sample is collected) if this occurs and for patients with HIV-1 RNA >500 copies/ml
- Plasma sample for potential HIV-1 gp160 sequencing upon treatment failure only (as defined in the protocol)
- Review dosing compliance
- Dispense study medication

Pregnancy: All female patients of childbearing potential will be tested throughout the study, using either a blood or urine sample, to ensure they are not pregnant.

Also as part of this study, a blood sample will be collected for human genetic analysis. Part II of this document describes this testing in more detail. This sample will be collected along with other blood samples for the study, and will not involve an extra needle stick. Genes contain the instructions for things such as hair and eye color, and for activities in the body such as how you respond to a drug. Because everyone’s genes are different to some degree, the scientific information we get from studying your genes and those of other study subjects may help us understand why people respond differently to the study drug. Your sample will be kept until all studies needed to get the study drug approved for sale are completed. Then, the sample will be destroyed. The analysis of this material is important for regulatory acceptance of UK-427, 857 as a new drug. Genotyping samples will be collected from all subjects unless prohibited by local regulations. If you are unable to agree to the genetic analysis for the CCR5 gene and live in a country where local regulations allow this collection, you will not be eligible to participate in this study.

The total blood loss (due to blood sampling) during the study will be approximately 50ml (approximately 20 tablespoons) per month. Your body will easily replace that amount during the study.

If you undergo a spinal tap as part of your routine care of your HIV infection during the study, cerebrospinal fluid samples will be forwarded to the sponsor for measurement of UK-427,857 levels.
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Alternative Treatment
Other treatments are available for treating HIV. Should you not wish to take part, the study doctor will explain what alternative treatment(s) is/are available to treat HIV. These treatments include approved and investigational drugs. The doctor will discuss with you the good points and bad points of the other treatments for HIV.

EXPECTED DURATION OF THE STUDY AND NUMBER OF SUBJECTS EXPECTED TO PARTICIPATE

You will be in the study for about 48 weeks. This study will involve approximately 90 centers in the United States and Canada with about 600 people. About 10-15 people are expected to participate at the University of Pennsylvania.

STUDY RESTRICTIONS/SUBJECT RESPONSIBILITIES

Study Medication/OBT
UK-427,857/placebo will be supplied by the sponsor. It may be taken with or without food. You will be asked to bring unused UK-427,857/placebo tablets to each study visit. You are responsible for supplying the OBT (other HIV drugs) prescribed by your study doctor. These antiretroviral agents used for your background regimen should be brought with you to the baseline (Day 1) visit and taken on that day and all days thereafter according to the manufacturer’s product labeling. You will be provided with a medication diary to track dosing information. It is very important that you stick to your dosing schedule and report any side effects to your study doctor or study staff. Do not change doses or stop medications without first speaking to study personnel.

Other Therapies
While you are on this study, it is important that you should not use any medications ("over the counter," prescription, or illegal) without approval from your study doctor. In addition, the following specific agents should not be taken during the study period: grapefruit, grapefruit juice, and alternative treatments including St. John’s Wort, or other herbal and food supplements. The only exceptions are paracetamol (a pain reliever) and multivitamins. New therapies or medications may be identified at a later point that would need to be added to the list of agents that should not be taken during the course of the study. If Efavirenz is given without the addition of either a protease inhibitor or delavirdine as part of (OBT), then the following drugs should not be used:

➢ If you are not on a protease inhibitor or delavirdine as part of your OBT regimen, then subjects should avoid ketoconazole, itraconazole, miconazole, clotrimazole, troleandomycin, nefazadone, and clarithromycin. The use of rifampin (rifabutin) for the treatment of a mycobacterial infection may be considered following consultation between the clinician and Pfizer medical monitor.

Pregnancy/Breastfeeding
Although initial in vitro (test tube) and animal studies indicate a low risk for reproductive toxicity (birth defects), at this stage of the development of UK-427,857, we do not know if the drug may have adverse effects on an unborn baby. It is therefore VERY IMPORTANT that if you are pregnant, plan to
become pregnant within at least 1 month of the end of the study, or are breast-feeding, YOU DO NOT TAKE PART in this study. Because the potential effects of UK-427,857 on sperm are not fully known at this time, men should use a condom to decrease the chances of both HIV transmission and pregnancy.

Side Effects
If you experience any symptom, complaint, side effect, pregnancy, or injury during the study, report it to a study doctor or study staff immediately.

It is your responsibility to report to study physician all changes in your physical or mental condition during the study. If you are not completely truthful with your study doctor regarding your health history, you may harm yourself by participating in this study. If you become ill and need to take any medicine, please communicate with the clinic immediately; you will be advised of what treatment may be acceptable, or you may be advised that you have to be withdrawn from the trial. It is important to tell the study physician if you have any side effects or adverse events during the course of the study.

Private Medical Insurance
If you have private medical insurance you should check with your insurers to ensure that your participation will not affect your medical insurance before agreeing to take part in the trial.

STUDY MEDICATION
Open-label Maraviroc (UK-427,857) will be supplied as 150 mg and 300 mg tablets during the observational phase of the study. You will receive one or two bottles per month of open label Maraviroc depending on the optimized background therapy. The dose of Maraviroc is 150mg twice a day, 300mg twice a day or 600mg twice a day depending on your optimized background therapy.

Childproof Containers
Your study drug will be provided in a childproof package. If you feel that this will be hard for you to open and close, please tell the study doctor and other arrangements will be made. Please make sure that no one else uses your study drug. Please keep it away from your other drugs. Keep study drug out of reach of children.

POSSIBLE SIDE EFFECTS, RISKS, AND DISCOMFORTS

NEW FINDINGS
A 27 year old female, non-HIV infected subject was given UK-427,857 (maraviroc) 600 mg once per day as part of a clinical trial to study the toleration of a once per day dose. After receiving 14 days of maraviroc she started to have flu-like symptoms including fever, neck pain, enlarged lymph nodes, dizziness, weakness, and an itchy skin rash. Four days later these symptoms were still present and her blood tests showed liver abnormalities. Maraviroc was stopped at this stage. After stopping maraviroc, the liver tests became better and the subject recovered. Complicating the understanding of this case is the presence of an untreated bacterial throat infection (Streptococcus pyogenes pharyngitis) that may have contributed to her symptoms and laboratory abnormalities, as well as evidence of fatty liver (hepatic steatosis) with unclear cause. The sponsor considers this case to be a potential case of liver
toxicity with an allergic reaction (drug hypersensitivity syndrome) possibly related to maraviroc. If you have flu-like symptoms, fever, and a skin rash, contact your physician immediately.

One subject has developed rash and severe liver disease requiring liver transplantation in the A4001026 treatment naïve study. The subject had received maraviroc 300 mg per day for 5 days. The subject was also receiving other medications that can cause liver disease, including isoniazid, trimethoprim - sulfamethoxazole, and zidovudine/lamivudine (Combivir). The possibility that maraviroc may have contributed to the liver disease cannot be excluded. A review of the Pfizer maraviroc safety database through 15 October 2005 indicated that there were no other serious adverse events of “toxic hepatitis”. Approximately 820 patients have received maraviroc in the phase 2b/3 clinical trials and approximately 390 subject have received multiple dose maraviroc in phase 1/2a trials.

You have the right to withdraw from this clinical trial at any time. If after receiving this important new information you agree to continue participating in the trial, you will need to sign the last page of this consent form.

If you consent to continue you are requested to immediately inform you study physician if you have any of the following symptoms: flu-like symptoms (fever, nausea and malaise), fatigue, jaundice (yellowing of the skin and/or eyes), abdominal pain and rash.

Important new information has been discovered during this clinical trial that may have an impact on your continued consent to participate in this clinical trial.

As a result of review of the program by an Independent Data Safety Monitoring Board (DSMB), the following changes were made to the study for safety reasons:

- An additional sample of blood (about ½ teaspoons) will be collected at the randomization visit. This sample will be used to check how well your liver is functioning. If the test results are very different than the results of your screening visit, your doctor will discuss them with the Pfizer Medical Monitor to determine if other actions need to be taken and if you should be enrolled into the study.
- The drug isoniazid (a drug used to treat tuberculosis) cannot be used for new patients entering the study. During the study, if your doctor feels that you require treatment with Isoniazid, this will be discussed with the Pfizer Medical Monitor. If you are already enrolled into the study and you have been taking isoniazid prior to these changes, isoniazid can be continued.

New information has become available (March 2006) following a planned review of the maraviroc clinical program (which includes four clinical trials) by an Independent Data Safety Monitoring Board (DSMB), and has resulted in changes to some of the existing clinical trials. As an ongoing participant in the maraviroc program you should be informed of these findings.

- In a different maraviroc study (A4001026) in treatment naïve patients, the DSMB recommended discontinuation of one of the two maraviroc treatment dose groups (300 mg once daily), because it did not meet very specific statistical requirements. There were no new safety concerns associated with this recommendation. The DSMB recommended that
patients who were receiving maraviroc 300 mg once daily in this trial have the option to change to twice-daily dosing of maraviroc. The DSMB has recommended no changes to the study you are participating in, including the once daily dose treatment group.

- Use of tipranavir as part of the optimized background therapy in this study was stopped for a period of time while the DSMB reviewed the data from patients on this therapy. The DSMB has now removed this restriction and tipranavir will be allowed as part of the optimized background therapy.

- There have been reports of serious skin reactions in patients who have received study medication. In the two instances reported at this time, there have been other medications implicated as the cause. However, since skin rashes are not included in the list of possible side effects that you reviewed as part of previous consent forms, it is important for you to be aware that skin reactions, such as rashes, blisters, and peeling are possible. If you develop a skin rash while on the study, please contact the study coordinator to discuss further evaluation.

SIDE EFFECTS

General
To date, UK-427,857 has been administered as a single dose up to 1200mg to healthy volunteers. The drug was very well tolerated up to the dose of 900mg with tiredness being the main complaint. This dose is three times higher than the unit dose we will be using in this trial. At the dose of 1200mg, in addition to tiredness, which was the most frequent side effect, there was a drop in standing blood pressure (postural hypotension) and headaches. Other side effects such as blurred vision or dry mouth were noted. All these effects resolved.

In addition, UK-427,857 has been administered in multiple doses for periods of 8-28 days in doses up to 1200mg daily. To date, there have been 501 healthy volunteers and 66 HIV positive subjects who have received at least one dose of UK-427,857. Data from both single dose and multi-dose studies have been consistent showing the most common adverse events reported following UK-427,857 dosing have been headache, dizziness, rhinitis, asthenia (tiredness), nausea and postural hypotension (low blood pressure). In addition to these adverse events, HIV positive subjects experienced gingivitis (infection of gums) and diarrhea. Postural hypotension appears to be the dose limiting adverse event. Although occurring infrequently at lower doses, it occurs more frequently than with placebo when subjects take individual doses of 600mg and above. These doses are higher than those being used in this study. There have been no deaths or serious adverse events reported in the Phase I program and most adverse events were judged to be mild or moderate in severity.

Heart
The ECG or electrocardiogram is a painless recording of the heart’s electrical activity and small changes in your heart’s activity can be monitored using an ECG. The QTc interval is one of the measurements of the ECG. Some drugs have been shown to make the QTc interval longer, which in rare cases could cause abnormal heart rhythms. UK-427,857 has been shown to have a small effect on the QTc interval which may lead to an abnormal heart rhythm at the highest dose (1200mg) tested so
far. A study designed specifically to evaluate the risk of QTc prolongation with UK-427,857 tested single doses of up to 900 mg and showed no significant effect on QTc interval. In addition, a 28-day multi-dose safety study was performed with ECG monitoring with doses including 300mg twice per day. No significant QTc intervals changes were noted in these healthy volunteers. In addition, no evidence of QTc prolongation has been observed in HIV positive subjects treated with UK-427,857. Effects on the QTc interval will be monitored in this study by doing ECGs at specific time points.

Liver
Liver enzyme abnormalities were seen in a single study with UK-427,857, but were not seen in other studies. Specifically, a 28 day study was performed to monitor the affect of UK-427,857 on liver function in doses including 300mg twice per day. There was no evidence of liver enzyme abnormalities during the 28 days dosing period and follow up. Your liver function tests will be closely monitored during this study.

Resistance
With any study where a drug against HIV is given on its own there is a potential risk that resistance will develop. However, laboratory experiments with UK-427,857 have indicated that resistance of the virus to UK-427,857 is likely to develop slowly.

Switch from CCR5 tropic to CXCR4 tropic HIV
There is a risk that treatment with a CCR5 blocker may cause the virus to use CXCR4 more rapidly. The test for determining coreceptor tropism has been validated in the laboratory but has not been clinically validated in a long-term clinical trial. In our early single drug trials, the assay correctly excluded the presence of X4 virus in 97% (63/65) of patients. Therefore, the sensitivity of the test for detecting small amounts of HIV that use an alternative co-receptor is not 100% and may not detect a small amount of CXCR4 virus. After taking a CCR5 inhibitor, there might be a risk to shift tropism to CXCR4 and progression to an AIDS defining event. The risk of this happening is currently unclear, but a change to CXCR4 HIV occurred in two subjects treated with UK-427,857 during a 10 day trial. Analysis from one individual on Day 11 showed HIV 1 that used the CXCR4 receptor. By day 40, the subject’s HIV had changed back to the CCR5 receptor. In the second subject, HIV that uses either the CCR5 or CXCR4 receptor (dual tropic virus) emerged by Day 11 and continues to be present after a little more than one year. This subject remains well with a viral load not different than baseline. The subject’s CD4 count is significantly lower than the lowest value prior to enrolling in the 10-day trial. He has now started antiretroviral therapy more than one year after the study. Whether the drop in CD4 count is due to the emergence of X4 virus or simply the natural disease progression is unknown. In this study careful screening will be done to make sure that your virus uses CCR5 when you enter the study. The tropism of your virus and the viral load (amount of circulating virus) will also be monitored during the study (and follow-up so that another regimen can be quickly initiated if the one you are on is not working.

Immune System
UK-427,857 blocks CCR5. CCR5 has many different functions in a normal immune system and blocking it with UK-427,857 may have an effect on the immune system and the way you respond to infections. However, approximately 1-2% of Caucasian individuals who have CCR5 receptor that does not work are healthy with no overt immune system problems.
Thyroid
In pre-clinical studies, UK-427,857 was given to rats at a dose of 300 mg/kg/day. This dose induced follicular cell hypertrophy (increase in size of the cells) in the thyroid and changes in thyroid hormone levels (decreased T4, and increased TSH). These findings were reversible when dosing was stopped. This is the only thyroid finding in animals including multiple dose studies in dogs and macaques (monkeys). Thyroid tests will be checked before and during the study.

Kidney
In one previous UK-427,857 trial, an increase in creatinine (measure of kidney function) has been observed in the 900mg per day - 1200mg per day treatment group. Four subjects receiving UK-427,857 1200mg per day had elevated creatinine values of 1.3 times above normal after 7 days of dosing. The same elevation occurred in the one subject who received placebo. Creatinine levels returned to normal after the drug was stopped. No similar increases in creatinine have been noted in other studies where subjects received the same or lower amounts of the drug.

Other
Subjects taking UK-427,857 at doses of 900mg and above have reported redness, burning, and eye pain. These events have not caused subjects to discontinue treatment and have tended to be mild (occasionally moderate), and self-limiting. Patients taking UK-427,857 at doses of 600mg and above, have reported experiencing abnormal or blurred vision which resolved within hours. These symptoms were reported more frequently in patients on active therapy than those receiving placebo. No patients discontinued treatment due to symptoms of abnormal vision.

Also, important new information has been discovered in another clinical trial that may have an impact on your continued consent to participate in this clinical trial.

Any drug can cause an allergic reaction, which if not treated promptly, could become life threatening. Maraviroc contains soy lecithin. Therefore if you had a history of allergy to soya or peanut you may develop an allergic reaction to maraviroc. In consequence you should not take maraviroc nor participate in this study. If you are already taking maraviroc, you should discuss the risks and benefits of continuing maraviroc. Should you develop such an allergic reaction to maraviroc while you are participating in this study please inform your doctor immediately.

Finally, other side effects that are not known at this time could occur during your participation in the study. All drugs have a potential risk of an allergic reaction, which if not treated promptly, could become life threatening. You will be informed of any changes in the way the study is done and of any newly identified risks to which you may be exposed. Significantly, initial results from an ongoing study in HIV infected patients indicate that UK-427,857 significantly reduces viral load during a short 10-day monotherapy without an increase in side effects.

RISKS
CHILDBEARING POTENTIAL
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WOMEN
Although initial animal studies indicate a low risk for birth defects, we do not know if the drug may have adverse effects on an unborn baby. Negative animal studies do not rule out an effect in humans. It is therefore VERY IMPORTANT that if you are pregnant, plan to become pregnant within at least 1 month of the end of the study, or are breast-feeding, YOU DO NOT TAKE PART in this study. To take part in this study you will be asked to use at least two acceptable birth control methods both during the trial and for at least 1 month after the end of the trial. Acceptable contraception includes, but is not limited to, oral hormone therapy, IUD, condoms, documented history of surgical sterilization, hysterectomy or partner vasectomy. Unacceptable contraception includes, but is not limited to, withdrawal method, rhythm method, or spermicides. Within these limits, the specific form of contraception employed is left to your discretion following discussion with the clinical staff and/or your family doctor (i.e. General Practitioner or Primary Care Physician).

Before the study, a pregnancy test is done for all women. This test might not detect an early pregnancy. Pregnancy tests may be repeated during the study. If you think you are pregnant, tell the study doctor immediately. A blood test to confirm you are not pregnant will be carried out at screening. A urine pregnancy test will be performed prior to dosing on Day 1 and during all following visits except for week 2. A blood test may also be done when indicated to confirm urine test results.

Women are also advised not to be breast feeding during this study as it is unknown whether UK-427,857 may pass into the breast milk and could be a risk to a nursing child.

If you become pregnant during the study, you may be discontinued from study participation for safety reasons. If you become pregnant within 28 days after you have stopped taking study drug, we ask that you contact your study doctor for safety monitoring. In either case, please make your obstetrician aware of your study participation. Your study doctor will ask that you, or your obstetrician, provide updates on the progress of your pregnancy and its outcome. The study doctor will make this information available to the study sponsor for safety monitoring follow-up.

Infants exposed to Maraviroc during pregnancy may be referred to a follow-up study if available in your region. Infants will not be followed for 18 months within this study as previously stated.

MEN
If you are a male, you will be required to use adequate birth control measures during your participation in the study as the potential effects of UK-427,857 on sperm are not fully known at this time. If your spouse or partner thinks they are pregnant during the study, tell your study doctor immediately. Men should use a condom to decrease the chances of both HIV transmission and pregnancy. Medically acceptable birth control methods include the following:
- Condom and spermicide
- Diaphragm and spermicide

If your spouse or partner thinks she is pregnant during the study or within 28 days after you have stopped taking study drug, tell your study doctor immediately. If your partner becomes pregnant, she will be asked to sign a release of information form to allow your study doctor to contact her obstetrician to collect updates on the progress of the pregnancy and its outcome. The study doctor will make this information available to the study sponsor for safety monitoring follow-up.
DISCOMFORTS
In order to obtain a sample of your blood, you may experience some minor discomfort with the insertion of the needle to draw your blood. Possible side effects from blood drawing include faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. There is also the slight possibility of infection.

COMPENSATION / RESEARCH RELATED INJURY
There is no direct compensation to subjects in this study. However, to cover parking, transportation and childcare, etc. expenses, you will be given $25.00 at each visit you attend.

Pfizer Inc may use information from this study to develop products or processes from which they may derive a profit. Pfizer Inc intends to retain exclusive rights to products or processes that are developed using information from this study, including samples you have donated. There are no plans to compensate you for any products developed from this research.

Medical care will be provided for any physical injury or illness that occurs as a direct result of your participation in this study. Medical care will be arranged through Dr. Pablo Tebas. This medical care will be at no cost to you. Pfizer Inc will pay the reasonable costs of this care. For this policy to apply, you must follow all directions and medical advice. You must do nothing to cause or contribute to this injury. Payment for such things as lost wages, disability or discomfort is not available. You will not give up any of your legal rights by signing this form.

There will be no charge to you for your participation in this study. The study drug, study related procedures, and study visits will be provided at no charge to you or your insurance company.

POSSIBLE BENEFITS OF THE STUDY
You have an 80% (4 out of 5) chance of getting UK-427,857 in addition to an OBT as part of your dosing regimen (either 150mg once a day or 150mg twice daily). This means 20% (1 out of 5) people will receive a placebo/dummy drug in addition to the optimized background therapy. You may have a good response to the treatment. All subjects may benefit from being given OBT. The information from this trial may help us to treat future subjects with HIV better. There is no guarantee that you will benefit from participating in this study.

INVESTIGATOR COMPENSATION
This study is being conducted for Pfizer, Inc. Pfizer, Inc is paying your study doctor to conduct this clinical trial.

REMOVAL FROM THE STUDY
UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

CONSENT FORM FOR Pfizer A4001027, Amendment 5, 17 June 2008: UK-427,857 in TREATMENT-EXPERIENCED HIV+ SUBJECTS

Your participation in this study may be stopped at any time without you being asked. Your participation in this research trial could be stopped by your doctor or the sponsor (Pfizer) for any of the following reasons:

- An adverse event or laboratory abnormality requiring drug discontinuation;
- Pregnancy;
- Planned enrollment into another study (including, but not limited to intervention, laboratory, psychological, or investigational drug, device, or biological studies);
- Treatment failure
- If continued participation is not in your best interest and is potentially dangerous to your well being
- The study is terminated by Pfizer;
- Noncompliance in taking your medication or in meeting your scheduled visits
- Lack of compliance with administration of study medication or with protocol procedures and instructions as given to you by your study doctor or nurse

If you meet the criteria for treatment failure or discontinue for another reason (e.g., pregnancy, adverse event), you will be followed until the Week 96 visit as per protocol guidelines and undergo the same procedures as if you were still on study drug. Your doctor, based on the results of resistance testing, will select the new regimen. Depending on these results you may be eligible to receive unblinded UK-427,857.

If you are taken out of the study, you will be asked to return any unused drug and you may undergo some tests as outlined in the study visit schedule.

The tests are to protect your safety. Your study doctor may also recommend other treatments.

RIGHT TO WITHDRAW FROM THIS STUDY

It is up to you to decide whether or not to take part. If you do decide to take part you will be asked to sign this consent form, and you will receive a copy of your signed form. If you decide to take part you are still free to withdraw at any time and without giving a reason. This will not affect the standard of care you receive. Choosing not to take part or leaving the study will not result in any penalty. You will not lose any benefits to which you are otherwise entitled. Your decision will not affect your access to medical care in the future. However, if you have received study treatment, we would like you to attend a post-treatment visit to ensure your safety.

If you are taken out of the study, you will be asked to return any unused drug and you may undergo some tests as outlined in the study visit schedule.

The tests are to protect your safety. Your study doctor may also recommend other treatments.

CONFIDENTIALITY AND PRIVACY RIGHTS
UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

CONSENT FORM FOR Pfizer A4001027, Amendment 5, 17 June 2008;
UK-427,857 in TREATMENT-EXPERIENCED HIV+ SUBJECTS

You are authorizing access to your medical records and every attempt will be made by investigators to maintain all information collected in this study strictly confidential, except as may be required by court order or by law. Authorized representatives of Pfizer and Quintiles, Inc. (monitors and auditors), the University of Pennsylvania Institutional Review Board (IRB) who approved the study, the Food and Drug Administration (FDA), possibly other US government agencies, and possibly government health agencies of other countries will have access to your medical records and may copy them. This access is necessary to insure the accuracy of the findings and your safety and welfare. If any publication or presentation results from this research, you will not be identified by name.

The ways your study doctor will use your study-related health information and the people who may receive it are identified in a separate form entitled “Research Subject Authorization Confidentiality and Privacy Rights.” You will be asked to sign that form to show that you give permission for these uses and sharing of your information. You do not have to sign the authorization form. However, if you do not, you will not be able to participate in the study.

PUBLIC HEALTH RESPONSIBILITY
Pennsylvania state law requires health care workers report the names of people who test positive for HIV, syphilis, gonorrhea or chlamydia to the Health Department. The reason for this is to make sure people who have these infections get treatment and that others exposed to these infections get tested. If you want, the research staff will help you with talking to the Health Department staff.

QUESTIONS OR PROBLEMS
If you wish further information regarding your rights as a research subject, you may contact the Director of Regulatory Affairs at the University of Pennsylvania by telephoning (215) 898-2614. If you ever have questions pertaining to your participation in this research study or about research-related injuries, you may contact the investigators or study nurse listed on the first page of this form.

PRIMARY CARE PHYSICIAN/SPECIALIST NOTIFICATION OPTION

Please indicate below whether you want us to notify your primary care physician or your specialist of your participation in this study.

________ Yes, I want the study doctor to inform my primary care physician/specialist of my participation in this study.

________ No, I do not want the study doctor to inform my primary care physician/specialist of my participation in this study.

________ I do not have a primary care physician/specialist.

________ The study doctor is my primary care physician/specialist.
UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

CONSENT FORM FOR Pfizer A4001027, Amendment 5, 17 June 2008:
UK-427,857 in TREATMENT-EXPERIENCED HIV+ SUBJECTS

CONSENT

- You have read (or someone read to you) changes to this Informed Consent Document, which details the new information regarding transition to the observational phase, Maraviroc dosing and long term follow up of infants exposed in-utero to Maraviroc.
- You have had time to review this information.
- You have been offered a chance to ask questions.
- You got answers to your questions that you are satisfied with.
- If you do not take part in the study you will not lose any benefits.
- If you leave the study you will not lose any benefits.
- If you leave the study you will not lose any legal rights.
- Your participation in this study is completely voluntary.

You will get a copy of this signed and dated Informed Consent Document for your records.

You have the right to withdraw from this clinical trial at any time. If after receiving this important new information you agree to continue participating in this trial in the observational phase, please indicate so, by signing the consent form below:

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<th>Study Doctor/Designee’s Name:</th>
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UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

CONSENT FORM FOR Pfizer A4001027, Amendment 5, 17 June 2008: UK-427,857 in TREATMENT-EXPERIENCED HIV+ SUBJECTS

A4001027 STUDY VISIT SCHEDULE

Screening (Day -42 to -28)
- Informed Consent
- Orthostatic Blood Pressure Monitoring
- Lab including: CD4/CD8, Viral Load, Viral Resistance, Co-receptor Tropism (Phenotype), Chemistry/Hematology, Hepatitis Screen, and Pregnancy Test

Randomization (Day -7 To -4)
- Review of screening tests to confirm eligibility
- Selection of Optimized Background Therapy
- Lab including: Viral Load

Baseline (Day 1)
- Physical Exam including medical history, electrocardiogram, vital signs, weight and height
- Orthostatic Blood Pressure Monitoring
- Lab including: Chemistry/Hematology, CD4/CD8, Viral Load, Co-receptor Tropism (Genotype/Phenotype), PBMC/Proviral DNA storage, Fasting Metabolic Assessment, Thyroid, and Host Genotype
- Hepatitis C Virus RNA (only if Hepatitis C antibody positive)
- Urinalysis (includes Pregnancy Test if female)
- Study Medication dispensed
- Review of Optimized Background Medications

Week 2
- Orthostatic Blood Pressure Monitoring
- weight
- Lab including: Chemistry/Hematology, CD4/CD8, Viral Load, and PK Sampling
- Review of Study and Optimized Background Medications

Weeks 4, 8, 12, 16, 20, 32, 40
- Targeted physical exam, vital signs, weight
- Lab including: Chemistry/Hematology, CD4/CD8, Viral Load, Co-receptor Tropism (Phenotype weeks 4, 8, 16, 32, 40 only), PBMC/Proviral DNA Storage, and PK Sampling (PK weeks 4, 8, 12, 16, 20 only)
- Hepatitis C Virus RNA (only if Hepatitis C antibody positive, week 12 visit)
- Urine Pregnancy Test (females)
- Dispense Study Medication
- Review of Study and Optimized Background Medications

Weeks 24, 48, And Early Termination
- Physical Exam including medical history, electrocardiogram, and vital signs
- Orthostatic Blood Pressure Monitoring
- Lab including: Chemistry/Hematology, CD4/CD8, Viral Load, Viral Resistance, Co-receptor Tropism (Genotype/Phenotype), PBMC/Proviral DNA Storage, Fasting Metabolic Assessment, Thyroid, and PK Sampling (PK at 24 weeks only)
- Hepatitis C Virus RNA (only if Hepatitis C antibody positive)
- Urinalysis (includes Pregnancy Test if female)
- Dispense Study Medication (week 24)
- Review of Study and Optimized Background Medications

Follow-up Visits After Week 48 to End of Study:
- Targeted physical examination and vital signs.
- Assessment of signs, symptoms and adverse events

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CONSENT FORM FOR Pfizer A4001027, Amendment 5, 17 June 2008:
UK-427,857 in TREATMENT-EXPERIENCED HIV+ SUBJECTS

- Review of concomitant medications
- Serum chemistry and hematology
- Hepatitis C virus RNA if you were Hepatitis C antibody positive at screening
- CD4 and CD8 lymphocyte determinations (absolute and percent);
- Plasma HIV-1 RNA level as determined by the Roche Amplicor HIV-1 MONITOR tests, standard method (if the results of the standard method are <400 copies/ml, the ultrasensitive method will automatically be performed)
- Blood sampling for preparation of two 1 ml plasma aliquots (frozen) stored for future testing
- Urine Pregnancy test for Women of Childbearing potential. A positive urine test will require a confirmatory serum pregnancy test.
- Plasma sample for HIV-1 co-receptor tropism phenotype as determined by the Monogram Biologics recombinant virus entry assay upon treatment failure as defined in the protocol, (this sample is to be drawn when the confirmatory plasma HIV-1 RNA sample is collected) if this occurs and for patients with HIV-1 RNA >500 copies/ml
- Plasma sample for potential HIV-1 gp160 sequencing upon treatment failure only (as defined in the protocol)
- Review dosing compliance
- Dispense study medication
UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

CONSENT FORM FOR Pfizer A4001027, Amendment 5, 17 June 2008:
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Part II to Consent (pages 18-21) GENOTYPING

NATURE AND PURPOSE OF THIS STUDY

The main part of this consent form describes the study with UK-427,857. This part asks for your consent to use a small sample of your blood to study your genes. This sample will be collected along with other blood samples for the study, and will not involve an extra blood draw. If you are unable to agree to the genetic analysis for the CCR5 gene and live in a country where local regulations allow this collection, you will not be eligible to participate in this study.

Genes contain the instructions or materials for things such as hair and eye color, and for activities in the body such as how you respond to a drug. Because everyone's genes are different to some degree, the scientific information we get from studying your genes and those of other study subjects may help us understand why people respond differently to the study drug. In this study, we will study your CCR5 gene, including whether you have the delta 32 form. Apart from the CCR5 gene, other genes will control how well the study drug works or whether you have a side effect. For example you have genes that control how well you break down and transport drugs in the body. Your genes may also control how the study drug affects other activities in the body such as blood pressure. If we see that a number of people in the study have an unexpected response to the study drug or the same side effect then, it may be necessary to genotype those genes we think may be involved. The information we get from these genes will only be used to help us understand the results of this trial. For example, the CYP3A5, CYP3A4 and MDR1 genes are related to the break down and transport of drugs in the body. The ADRA1A and ACE genes are related to blood pressure. These genes and others like them may be studied to understand the amount of UK-427,857 in your blood, blood pressure changes or other responses people have to the study drug. Your sample will be kept until all studies needed to get the study drug approved for sale are completed. Then, the sample will be destroyed.

You may request the results of your CCR5 delta 32 test through your doctor. It is important for you to talk to your doctor about this test before you request the results. CCR5 delta 32 is one of many factors, which affect how you respond to being infected with HIV. The results of any other genetic analysis, such as on the CYP3A5, CYP3A4, MDR1, ADRA1A and ACE genes, will be used only to help us understand how you respond to UK 427,857. They will not affect your medical care, and will not be available to you or your doctor.

While used for research study purposes, your sample and genetic results will be treated confidentially, as described in the CONFIDENTIALITY section. The genetic results will be identified with your study ID number only, not your name. The link between your study ID number and your name will be held by the study doctor, and will be kept separate from your genetic results which are held by the study sponsor. If you request your CCR5 delta 32 test results, they may be placed in your medical record and identified with your name. If others obtain these results, such as an employer or insurance company, you could have unwanted financial, legal, emotional or social consequences. You should consider these possible risks carefully before deciding whether to request your CCR5 delta 32 test results.

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UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

CONSENT FORM FOR Pfizer A4001027, Amendment 5, 17 June 2008:
UK-427,857 in TREATMENT-EXPERIENCED HIV+ SUBJECTS

PROCEDURES

A small sample of blood (about 2 teaspoons) will be taken at the baseline visit, which will be used to
study the CCR5 gene. Your sample will be kept until all studies needed to get the study drug approved
for sale are completed. Then, the sample will be destroyed.

POSSIBLE RISKS AND DISCOMFORTS

The risks of blood sampling include possible discomfort and pain, minor bruising, and swelling at the
site of the needle stick.

POSSIBLE BENEFITS

You will not receive any direct benefit as a result of taking part in this research. However, the
knowledge gained from this research may benefit others.

CONFIDENTIALITY

All information concerning the confidentiality, use and disclosure of your health information contained
in the University of Pennsylvania's HIPAA Authorization Form applies to this Addendum as well, with
the exception that information from this genetic research will only be used for the purposes outlined
above.

SAMPLE OWNERSHIP

The study sponsor will not sell or transfer ownership of the sample to other parties. The samples will
be used only by Pfizer Inc and/or researchers working with Pfizer Inc, and only for the research
described above. Pfizer Inc may use information from your sample to develop products or processes
from which they may derive a profit. Pfizer Inc intends to retain exclusive rights to products or
processes that are developed using information from your sample. There are no plans to compensate
you for any products developed from this research.

INJURY/COMPLICATIONS

Medical care will be provided for any physical injury or illness that occurs as a direct result of your
participation in this study. Medical care will be arranged through Dr. Pablo Tebas. This medical care
will be at no cost to you. Pfizer Inc will pay the reasonable costs of this care. For this policy to apply,
you must follow all directions and medical advice. You must do nothing to cause or contribute to this
injury. Payment for such things as lost wages, disability or discomfort is not available. You will not
give up any of your legal rights by signing this form.

IC V10 10/10/08
There will be no cost to you for any procedure performed as part of this research.

WITHDRAWAL FROM THIS RESEARCH

If you change your mind about participating, you can withdraw your sample by making a request to the study doctor.

OFFER TO ANSWER QUESTIONS ABOUT THIS RESEARCH

Before you sign this form, you should ask questions about anything that you do not understand. The study staff will answer questions before, during, and after the study.

If you wish further information regarding your rights as a research subject, you may contact the Director of Regulatory Affairs at the University of Pennsylvania by telephoning (215) 898-2614. If you ever have questions pertaining to your participation in this research study or about research-related injuries, you may contact the investigators or study nurse listed on the first page of this form.
CONSENT FORM FOR Pfizer A4001027, Amendment 5, 17 June 2008:
UK-427,857 in TREATMENT-EXPERIENCED HIV+ SUBJECTS

CONSENT for ADDITIONAL RESEARCH

- You have read (or someone read to you) this Informed Consent Document.
  - This document describes the purpose and nature of this study.
  - This study includes genetic analysis of the CCR5 gene and other genes in relation to how
    people respond to the study drug.
- You have had time to review this information.
- You have been offered a chance to ask questions.
- You got answers to your questions that you are satisfied with.
- If you do not take part in the study you will not lose any benefits.
- If you leave the study you will not lose any benefits.
- If you leave the study you will not lose any legal rights.
- Your participation in this study is completely voluntary.

You will get a copy of this signed and dated Informed Consent Document for your records. You agree
to participate in this study. It is your responsibility to tell the study doctor about all changes in your
physical or mental health during the study.

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