

UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

Gilead Sciences, Inc

GS-US-292-0112, Amendment 1, 20-AUG-2013; Addendum 2, 13-DEC-2013

A Phase 3 Open-label Safety Study of Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide Single-Tablet Regimen in HIV-1 Positive Patients with Mild to Moderate Renal Impairment

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

Your contacts for this study at the Hospital of the University of Pennsylvania [HUP] are:

Site address: 502 Johnson Pavilion, Philadelphia, PA 19104

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24 Hour Emergency Number (215) 662-6059 Ask for the Immunodeficiency Program Doctor on call

NEW INFORMATION

In the Subject Informed Consent Form you signed when you agreed to take part in this research study, you were told that you would be informed if there was new or updated information related to the study. This revised consent form provides updated information below regarding the risks associated with **EVG/COBI/FTC/TAF (E/C/F/TAF)**; this has also been inserted into the main body of the consent on page 8. In addition, the blood volume for persons needing to come back to confirm viral load values has been corrected (pages 4, 6, 7 and 8) from 12 ml (2 ½ teaspoons) to 24 ml or 5 teaspoons.

E/C/F/TAF is a fixed dosed combination pill (FDC, or “combination pill”) containing four medications: elvitegravir (EVG), cobicistat (COBI), emtricitabine (FTC), and tenofovir alafenamide (TAF).

The risk list (adverse events) for E/C/F/TAF FDC are updated based on data collected from two year-long clinical studies in which 866 subjects who had never been on treatment for their HIV infection received E/C/F/TAF FDC:

Very common (more than or equal to 10%):

- headache
- diarrhea
- nausea

Common ($\geq 1\%$ and $< 10\%$):

- vomiting
- abdominal pain
- dyspepsia (indigestion)
- flatulence (passing gas)
- rash
- fatigue

Tenofovir alafenamide is a new form of the anti-HIV drug, tenofovir. A study in dogs detected inflammation in the back portion of the eye (posterior uveitis) in some dogs when TAF was given at the highest doses. Across all Phase 2 and Phase 3 studies in which 2,394 subjects received E/C/F/TAF, eye disorders were uncommon, balanced between treatment arms, and most were considered by the investigator as unrelated to the study drugs. None were definitive for posterior uveitis, and none resulted in permanent discontinuation of study drugs. One subject in Study GS-US-292-0106 had an adverse reaction of intermediate uveitis (inflammation in the middle of the eye) that was considered related to study drug by the investigator but resolved while the subject continued on study drug without interruption. If you experience any visual disturbances or eye pain

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during this study, you should immediately report what you experienced to your doctor and be evaluated.

INTRODUCTION

You have been asked to take part in a clinical research study involving an experimental drug named Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide Single Tablet Regimen (E/C/F/TAF STR). An experimental drug means that the FDA has not approved it for use by the general public.

YOUR RIGHTS

This consent form tells you about the study. Your study doctor or study staff will go over this with you and answer any questions you may have regarding this study. You may also decide to discuss it with your family, friends, or family doctor. If you agree to volunteer, you will be asked to sign and date this consent form. You will be given a copy of the signed and dated consent form to keep.

No one can force you to take part in this study. Even if you agree to participate now, you are free to change your mind. You may stop at any time without penalty or loss of benefits which you would otherwise have.

Before you agree to volunteer, you must understand the purpose of the study, how your participation may help you, any potential risks to you, and what is expected of you during the study.

PURPOSE OF THE STUDY

The treatment of HIV infection requires the combination of several medications in order to decrease the amount of virus in the body, improve immune function and delay the progression of the disease. This has generally required patients to take a large number of pills each day, and many experience a loss of effectiveness of their current medication regimen over time or unacceptable side effects. Therefore, it is important to develop new drug regimens. In addition, the combination of drugs into a single tablet reduces the number of pills a patient has to take and makes it more convenient to stick to the prescribed drug regimen.

The purpose of this study is to see if the combination pill E/C/F/TAF is safe and effective in reducing levels of HIV-1 in the blood of subjects who have renal impairment, or in other words, kidney function problems. You have been asked to participate in this study because you have HIV and you have renal impairment. Safety and tolerability will be determined on the basis of physical exams, laboratory tests, bone scans and questions about any problems you might experience during the study.

This study also includes two types of pharmacokinetic analyses. "Pharmacokinetics or "PK"" is the study of actions a drug takes within the body including how it is absorbed by the body (such as through the mouth, stomach or intestine), how it moves throughout the body, how it is metabolized (processed, converted and used) by the body, and how it is removed from the body. As part of the main study, drug levels of the study drugs will be determined at various study visits. In addition, there is an OPTIONAL sub-study that is more comprehensive: drug levels are measured at multiple time points in a 24 hour period.

Pharmacokinetic (PK)/Pharmacodynamic (PD)/Peripheral Blood Mononuclear Cells (PBMC) Sub-study
PK is described above. Pharmacodynamics or PD is what the drug does to the body, for instance does the drug speed up or slow down as process. PBMCs are blood cells that are part of the immune system and fight infection; these cells include T cells (CD4 and CD8). The PK/PD/PBMC sub-study will be performed at three different visits: Baseline (PD only), at or between the Week 2, Week 4, or

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Week 8 and Week 24 (PD only). Approximately 30 subjects are expected to participate at selected study sites. The sub-study requirements are explained in a separate, additional Consent Form that will be reviewed with you. If you meet the requirements and wish to participate, you will sign this separate consent form.

DESIGN OF THE STUDY

If you agree to participate, you will be one of approximately 260 subjects. Some subjects will have had previous treatment for HIV and some subjects will not have been treated for HIV. About 5-7 subjects are expected to enroll at the University of Pennsylvania.

Once you are confirmed to be eligible to participate in the study, and you state that you want to take part in the study, you will be assigned a subject number.

If you have been previously treated for HIV, you will change your treatment medication to the study medication.

If you have never been treated for HIV, you will begin treatment with the study medication.

All of your study drug will be supplied by Gilead Sciences, Inc. who is also the sponsor of this study. Your study doctor or study nurse will review the proper storage of all study drug used in this study with you. **Study drug must be taken once a day, at the same time every day, with food.** It is very important that you take your study drug every day as instructed by the study doctor. There is one visit (at Weeks 2, 4 and/or 8) for which you may have to take the study drug in the study center and all other days you will take it on your own at home. You must bring the study drug bottles including any unused study drug with you at each clinic visit.

DURATION OF THE STUDY

The screening period (the time between the Screening visit and Day 1 [baseline] visit) may last up to 30 days. Once you are confirmed to be eligible to participate in the study, and you state that you want to take part in the study, your participation in this study will last about 96 weeks, not including the screening visit. Following confirmation of your eligibility, you will be required to visit the study center at least 14 times (at weeks 1, 2, 4, 8, 12, 16, 24 and then every 12 weeks through week 96).

Following your 96 weeks on-study, you will continue to take your study drug and attend visits every 12 weeks until the study drug becomes commercially available or the study sponsor, Gilead, ends the study.

If you decide to participate in the study, you can stop your participation at any time. Also, your participation in this study may be stopped at any time as described on the section "**WITHDRAWAL FROM STUDY AND REFUSAL TO PARTICIPATE**" of this consent form. This means that your participation in the study may be shorter than described above.

SUBJECT RESPONSIBILITIES

If you decide to be in this study, there are certain rules you must follow before, during, and after the study period. Some are listed below, but there could be others that the study doctor will discuss with you:

- It is very important not become pregnant or get someone pregnant during this study.
- It is very important that you tell your study doctors all of the information you know about your health and medications you may be taking throughout the study period. If you do not tell the study doctor everything you know, you may be putting your health at risk.

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- It is very important to return all of the used and unused study drug and/or empty bottles to the clinic at each visit.
- It is very important to follow all instructions given to you while you are participating in this study. If you do not, you may be removed from the study. If you are unsure about what you are supposed to do, ask the Study Doctor.
- Some insurance companies require people who are renewing a policy or getting a new policy to tell them about participating in a clinical study. You should check with your insurer to determine if taking part in this study will affect your existing insurance policy.

STUDY PROCEDURES

To help the study doctor determine your eligibility to participate in this study and whether it is safe for you to do so, you need to be seen at the study center within 30 days before the study starts. After you sign the informed consent form and receive a copy of the informed consent form, you will have screening procedures done. Note that all of the procedures listed below may not be performed if at any point during the evaluation you fail eligibility. These procedures will include:

- An interview about your medical history, including any illnesses or health problems, your history of HIV-1 disease-related events and prior medications within 30 days.
- A complete physical examination, vital signs, weight, and height.
- A 12-lead ECG (electrocardiogram) to check the functioning of your heart.
- A urine sample for laboratory tests.
- If you are a female able to become pregnant, a blood pregnancy test will be required. If the blood pregnancy test is positive, you will not be eligible to participate in the study.
- About 21 mLs (about 4 teaspoons) (5 mL = 1 teaspoon) of blood will be taken for general health screening tests and tests related to your HIV, such as chemistry, complete blood count, CD4+ (white blood cell that fights infection) cell count, tests for hepatitis B virus, hepatitis C virus, to measure the amount of HIV-1 virus in your blood, and kidney function tests
- If you have never had HIV treatment, about 24 mLs (about 4 ½ teaspoons) of blood will be drawn for an HIV-1 genotype test. Genotype testing is a technique that finds changes or “mutations” in certain regions of the HIV-1 gene. Some mutations can prevent certain anti-HIV drugs or drug regimens from reducing the level of HIV-1 in your blood. When this occurs, HIV-1 becomes “resistant” to that drug and possibly other similar drugs.

The study doctor will review all of your medical information and findings from your Screening visit (including medical history, medications, clinical laboratory results, physical exam, etc.) and other entry criteria, as required by the study protocol, to determine if you are eligible to participate in this study.

Day 1 (baseline) Visit:

You will be asked to come back to the study center within 30 days after the Screening visit for the Day 1 (baseline) visit. You must not have anything to eat or drink, except water, for at least 8 hours before the visit (fasted state). Eating or drinking may affect the results of your urine and blood testing. The following procedures will occur during this visit:

- You will be asked whether there has been any change in your health (illness or health problems) and whether you have taken any new medications since your last visit.
- A complete physical examination, vital signs and weight.
- Dual energy x-ray scan (called a DEXA scan) of your spine and hip (prior to taking study drug) will be done to measure the density of your bones.

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- A urine sample will be collected for laboratory tests and a storage sample for possible future testing. Some of the urine collected will be tested to see if the study drugs have any effect on your kidneys.
- If you are a female able to become pregnant, a urine pregnancy test will be required. If the urine pregnancy test is positive, a blood pregnancy test will be done to confirm the result; if confirmed, you will not be able to participate in the study.
- About 21 mLs (about 4 teaspoons) of blood will be taken for testing of chemistry, complete blood count, thyroid function (thyroid is a gland that makes hormones which regulate metabolism), kidney function tests, CD4+ cell count and to determine HIV-1 levels in your blood.
- About 10 mL (about 2 teaspoons) of blood will be taken for testing your bone health. If you have not fasted, you will be asked to return to the study center within 72 hours in a fasted state.
- Tests on blood being drawn at this visit will be used to measure changes in the amount of sugar and fats in your blood. About 4 mL (about 1 teaspoon) of blood will be taken for this test. It is important that your blood is drawn for this sample prior to eating (in a fasting state). If you have not fasted, you will be asked to return to the study center within 72 hours in a fasted state. "Fasting" means that you will not eat or drink anything except water for at least 8 hours before your blood is drawn.
- About 14 mL (about 3 teaspoons) of blood will be collected and stored to allow the possibility of conducting clinical tests at a later date (for example, to check whether the HIV in your blood can develop resistance to this anti-HIV drug).
- You will have a renal sonogram, which is an ultrasound test on your kidneys to look for any problems in your kidneys. It is normally a painless procedure and lasts about 30 minutes.
- You will be given instructions on how to take your study drug (i.e. with food and at the same time each day).
- You will receive study drug and will be asked to begin taking your first dose within 24 hours after the clinic visit.

Week 1 to Week 48 Visits:

You will be asked to return to the clinic for study visits at Weeks 1, 2, 4, 8, 12, 16, 24, 36 and 48.

At Weeks 1, 2, 4, 12, 24, and 48, you must arrive in a fasting state for your visit. "Fasting" means that you will not eat or drink anything except water for at least 8 hours before your blood is drawn. Eating or drinking may affect the results of your urine and blood testing. If you have not fasted, you will be asked to return to the study center within 72 hours in a fasted state.

The following procedures will occur during these visits:

- You will be asked whether there has been any change in your health (illness or health problems) and whether you have taken any new medications since your last visit.
- A physical examination, vital signs, and weight (a complete physical examination will be performed at Weeks 24 and 48; a symptom-directed physical examination will be performed at all other visits as needed).
- A urine sample for standard laboratory tests and storage sample for possible future testing. At weeks 1, 2, 4, 12, 24, and 48, some of the urine will be tested to see if the study drugs have any effect on your kidneys; at these visits it is important that you arrive in a fasting state. If you have not fasted, you will be asked to return to the study center within 72 hours in a fasted state.

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- If you are a female able to become pregnant, a urine pregnancy test will be required. If the urine pregnancy test is positive, you will have a blood pregnancy test to confirm the result. If the blood test is positive, you will be discontinued from study drugs.
- About 19 mLs (about 4 teaspoons) of blood will be taken for testing of chemistry, complete blood count, thyroid function, CD4+ cell count, kidney function tests and to determine HIV-1 levels in your blood.
- About 10 mL (about 2 teaspoons) of blood will be taken for testing your bone health. If you have not fasted, you will be asked to return to the study center within 72 hours in a fasted state (weeks 1, 2, 4, 12, 24 and 48)
- Tests on blood being drawn at Weeks 24 and 48 will be used to measure changes in the amount of sugar and fats in your blood. About 4 mL (about 1 teaspoon) of blood will be taken for this test. It is important that your blood is drawn for this sample prior to eating (in a fasting state). If you have not fasted, you will be asked to return to the study center within 72 hours in a fasted state.
- A 12-lead ECG (electrocardiogram) to check the functioning of your heart at weeks 24 and 48
- DEXA scan (x-ray) of your spine and hip will be performed at weeks 24 and 48.
- About 14 mL (about 3 teaspoons) of blood will be collected and stored to allow the possibility of conducting tests at a later date (for example, to check whether the HIV in your blood can develop resistance to this anti-HIV drug).
- Weeks 1-24, about 8 mL (about 1 ½ teaspoons) of blood will be taken to measure the amount of study drug in your blood. This type of testing is called pharmacokinetics (PK) and measures the amount of the study drug in your blood. It tells the researchers how much time it takes for the study drug to be absorbed into your body and how long it stays in your body after it has been absorbed. On these visit days you will be asked the time and date that you took your last dose of your study drugs.
- At the weeks 2, 4 and/or 8 visits, the pharmacokinetic (PK) testing will be done 15 minutes to 4 hours after you have taken your study drug. For this test to be accurate, it is important that you take your dose of study medication as directed by the study doctor.
- If you do not appear to be responding properly to the study drug, you may be required to return to the clinic for an unscheduled visit to confirm whether or not you are truly failing your study treatment. Approximately 24 mL (about 4 ½ teaspoons) of blood will be drawn during this visit to measure the amount of HIV-1 in your blood and for genotype/phenotype testing. Phenotype testing is a technique used to determine whether a mutation in the HIV-1 gene changes how anti-HIV drugs affect the HIV-1 virus. The study doctor will then decide whether or not a change to your study treatment regimen is required.
- You will receive a 4-week supply of study drug at Weeks 4, 8, and 12. You will receive an 8-week supply of study drug at Week 16. At Weeks 24, 36 and 48 you will receive a 12-week supply of study drug. All study medication should be taken once a day at the same time every day with food. You will be counseled regarding the importance of taking all study drugs.
- You will be required to bring your used and unused study drug bottles back to the clinic at each visit. The study drug (number of tablets) will be counted. You will be asked about any missed doses since your last visit.

Week 60 to Week 96 and every 12 weeks following Week 96:

You will be asked to return to the clinic for study visits at Weeks 60, 72, 84 and 96.

After the Week 96 visit you will be asked to continue coming in for study visits every 12 weeks until the study drug becomes commercially available or the study sponsor, Gilead, ends the study.

The following procedures will occur during these visits:

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- You will be asked whether there has been any change in your health (illness or health problems) and whether you have taken any new medications since your last visit.
- A physical examination, vital signs, and weight (a complete physical examination will be performed at Weeks 72 and 96; a symptom-directed physical examination will be performed at all other visits as needed).
- A urine sample for standard laboratory tests and storage sample for possible future testing.
- If you are a female able to become pregnant, a urine pregnancy test will be required. If the urine pregnancy test is positive, you will have a blood pregnancy test to confirm the result. If the blood test is positive, you will be discontinued from study drugs.
- About 18 mL (about 4 teaspoons) of blood will be taken for testing of chemistry, complete blood count, thyroid function, CD4+ cell count, kidney function tests and to determine HIV-1 levels in your blood.
- Tests on blood being drawn at Weeks 72, 96, every 24 weeks post Week 96 will be used to measure changes in the amount of sugar and fats in your blood. About 4 mL (about 1 teaspoon) of blood will be taken for this test. It is important that your blood is drawn for this sample prior to eating (in a fasting state). If you have not fasted, you will be asked to return to the study center within 72 hours in a fasted state.
- A 12-lead ECG (electrocardiogram) to check the functioning of your heart at Week 96.
- DEXA scan (x-ray) of your spine and hip will be performed at weeks 72 and 96.
- About 14 mL (about 3 teaspoons) of blood will be collected and stored to allow the possibility of conducting tests at a later date (for example, to check whether the HIV in your blood can develop resistance to this anti-HIV drug).
- If you do not appear to be responding properly to the study drug, you may be required to return to the clinic for an unscheduled visit to confirm whether or not you are truly failing your study treatment. Approximately 24 mL (about 5 teaspoons) of blood will be drawn during this visit to measure the amount of HIV-1 in your blood and for genotype/phenotype testing. Phenotype testing is a technique used to determine whether a mutation in the HIV-1 gene changes how anti-HIV drugs affect the HIV-1 virus. The study doctor will then decide whether or not a change to your study treatment regimen is required.
- At the Week 60 visit, you will receive a 12-week supply of study drug until it becomes commercially available or the study sponsor, Gilead, ends the study. All study medication should be taken once a day at the same time every day with food. You will be counseled regarding the importance of taking all study drugs.
- You will be required to bring your used and unused study drug bottles back to the clinic at each visit. The study drug (number of tablets) will be counted. You will be asked about any missed doses since your last visit.

Restrictions During the Study

You will be told not to eat or drink anything except water for at least 8 hours before your blood is drawn and your urine is collected at Day 1 (baseline) visit, Weeks 1, 2, 4, 12, 24, 48, 72, 96, every 24 weeks post Week 96 .

You cannot take any antacids that contain calcium, magnesium, or aluminum (for example, Tums® or Roloids®), Carafate® (an ulcer medicine), or vitamins/mineral supplements that contain calcium, iron or zinc for a minimum of 2 hours before and 2 hours after any dose of study drugs. You must check with the study doctor before taking any medication or health supplements for the length of the study.

Early Study Drugs Discontinuation (ESDD) Visit

If you discontinue study drug at any time before the study is complete, you will be asked to return to the study center within 72 hours of stopping study drugs. Procedures at this visit will include:

- You will be asked whether there has been any change in your health (illness or health problems) and whether you have taken any new medications since your last visit.
- A complete physical examination, vital signs, and weight.
- A urine sample for standard laboratory tests and storage sample for possible future testing. Some of the urine may be tested to see if the study drugs have any effect on your kidneys if your last test occurred more than 12 weeks before the ESDD visit. For this test it is important that you arrive in a fasting state. If you have not fasted, you will be asked to return to the study center within 72 hours in a fasted state.
- If you are a female able to become pregnant, a urine pregnancy test will be required. If the urine pregnancy test is positive, you will have a blood pregnancy test to confirm the result.
- About 18 mL (about 4 teaspoons) of blood will be taken for testing of chemistry, complete blood count, CD4+ (white blood cell that fights infection) cell count, thyroid function, kidney function tests and to determine HIV-1 levels in your blood. Some of the blood may be tested for your bone health if your last test occurred more than 12 weeks before the ESDD visit. For this test it is important that you arrive in a fasting state. If you have not fasted, you will be asked to return to the study center within 72 hours in a fasted state.
- About 14 mL (about 3 teaspoons) of blood will be collected and stored to allow the possibility of conducting tests at a later date (for example, to check whether the HIV in your blood can develop resistance to this anti-HIV drug).
- About 24 mL (about 5 teaspoons) of blood may be drawn for genotype/phenotype testing.
- A 12-lead ECG (electrocardiogram) to check the functioning of your heart.
- DEXA scan (x-ray) will be performed if the last scan was more than 12 weeks from the ESDD visit.
- You will be required to bring your used and unused study drug bottles back to the clinic.

30-Day Follow-Up

You will be asked to attend a 30-Day Follow-Up visit in the following cases:

- If you discontinue your study drug, and do not wish to continue attending regularly scheduled visits, you will be asked to return to the study center 30 days after the completion of the Early Study Drugs Discontinuation visit.

Procedures at this visit will include:

- You will be asked whether there has been any change in your health (illness or health problems) and whether you have taken any new medications since your last visit.
- A symptom-directed physical examination, vital signs and weight.
- A urine sample for standard laboratory tests and storage sample for possible future testing.
- If you are a female able to become pregnant, a urine pregnancy test will be required. If the urine pregnancy test is positive, you will have a blood pregnancy test to confirm the result.
- About 18 mL (about 4 teaspoons) of blood will be taken for chemistry, complete blood count, CD4+ (white blood cell that fights infection) cell count, thyroid function, kidney function tests and to determine HIV-1 levels in your blood.
- About 6 mL (about 1 teaspoon) of blood will be collected and stored to allow the possibility of conducting tests at a later date.

RISKS

EVG/COBI/FTC/TAF (E/C/F/TAF)

E/C/F/TAF is a single-tablet regimen (STR, or “combination pill”) containing four medications: elvitegravir (EVG), cobicistat (COBI), Emtriva® (FTC), and tenofovir alafenamide (TAF).

The risk list (adverse events) for E/C/F/TAF FDC are updated based on data collected from two year-long clinical studies in which 866 subjects who had never been on treatment for their HIV infection received E/C/F/TAF FDC:

Very common (more than or equal to 10%):

- headache
- diarrhea
- nausea

Common ($\geq 1\%$ and $< 10\%$):

- vomiting
- abdominal pain
- dyspepsia (indigestion)
- flatulence (passing gas)
- rash
- fatigue

Tenofovir alafenamide is a new form of the anti-HIV drug, tenofovir. A study in dogs detected inflammation in the back portion of the eye (posterior uveitis) in some dogs when TAF was given at the highest doses. Across all Phase 2 and Phase 3 studies in which 2,394 subjects received E/C/F/TAF, eye disorders were uncommon, balanced between treatment arms, and most were considered by the investigator as unrelated to the study drugs. None were definitive for posterior uveitis, and none resulted in permanent discontinuation of study drugs. One subject in Study GS-US-292-0106 had an adverse reaction of intermediate uveitis (inflammation in the middle of the eye) that was considered related to study drug by the investigator but resolved while the subject continued on study drug without interruption. If you experience any visual disturbances or eye pain during this study, you should immediately report what you experienced to your doctor and be evaluated.

In addition, more than 100 HIV-negative subjects have been treated with the E/C/F/TAF combination pill as part of a Phase 1 study to evaluate the level of each drug in the blood (pharmacokinetics). No deaths or serious side effects occurred during the study. One subject discontinued from the study because of increased creatine phosphokinase (CPK) (an enzyme produced by muscle cells) levels in the blood that was assessed as related to the study drug. The most frequently reported side effect was constipation. Other side effects included nausea, dizziness, headache, breast tenderness, and papular (raised bumps on skin) rash. No subject in any treatment arm developed any clinically significant changes on ECG throughout the study.

Elvitegravir (EVG)

As of 17 June 2012, a total of 327 HIV-1 infected subjects and 907 healthy subjects have been treated with EVG as an individual agent as part of Phase 1 and 2 clinical studies. In addition, approximately 354 HIV-1 infected treatment experienced subjects have been dosed in an on-going blinded Phase 3 study. Additionally, 194 healthy subjects and 48 HIV-1 infected ARV-naïve (never took antiretroviral treatment) subjects have been treated with EVG in a single tablet regimen containing elvitegravir (EVG), emtricitabine (FTC), tenofovir disoproxil fumarate (TDF) and COBI

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(cobicistat) as part of Phase 1 and 2 clinical studies. As of 10 April 2012, 916 HIV-1 infected subjects, both ARV treatment-naïve and ARV treatment-experienced, adult subjects have had also received elvitegravir as part of the E/C/F/TDF STR in ongoing Phase 3 studies.

The following adverse reactions have been identified for EVG: Very Common (more than or equal to 10%): diarrhea, nausea, fatigue and headache. Common (more than or equal to 1% and less than 10%): stomach pain (abdominal pain), indigestion (dyspepsia), gas (flatulence), vomiting, dizziness, abnormal dreams, depression, unable to sleep (insomnia), rash. Uncommon (more than or equal to 0.1% and less than 1%): abnormal kidney function test (increased blood creatinine), a certain type of kidney disease (Fanconi syndrome acquired), and kidney failure (renal failure

Cobicistat (COBI)

As of 10 July 2012, approximately 635 healthy subjects have been treated with COBI as an individual agent as part of 19 studies and 69 HIV-1 infected ARV treatment-naïve subjects have been treated with COBI in a study that is currently ongoing. In addition, 344 HIV-1 infected ARV-naïve subjects have received COBI as an individual agent in an ongoing, blinded study. 194 healthy subjects from 5 clinical studies, and as of 10 April 2012, 964 HIV-1 infected (ARV treatment-naïve and ARV treatment-experienced) have been dosed with COBI as part of the E/C/F/TDF STR.

No significant changes in serum immunoglobulins (antibodies), ECG, thyroid hormone levels or urine characteristics have been seen in clinical studies to date. In two ongoing studies in which approximately 100 HIV-positive subjects are receiving COBI, mild decreases in estimated kidney function were observed. A follow-up study in healthy subjects showed that actual kidney function does not change. This phenomenon is seen with two other commonly used FDA-approved drugs, trimethoprim (an antibiotic) and cimetidine (an antacid). Your kidney function will be closely monitored throughout your participation in this study with blood and urine tests.

No additional side effects for COBI have been observed in clinical studies of COBI as an individual agent in addition to those listed above for E/C/F/TDF STR.

Tenofovir alafenamide (TAF)

Tenofovir alafenamide (TAF) is a new form of the anti-HIV drug, tenofovir. TAF as an individual agent has been administered to more than 40 HIV-positive subjects in two separate studies. In study GS-US-120-1101, subjects received higher doses of TAF (50 mg and 150 mg) than the TAF dose in this study. Side effects that were seen in more than two subjects were headache, nausea, and gas (flatulence). In Study GS-US-120-0104, adverse events observed in more than two subjects were nausea and fatigue. One serious adverse event of chest pain was reported, but not considered related to study drugs. In addition, TAF has been given to over 83 HIV-negative subjects.

A study in dogs detected eye problems (posterior uveitis) in some dogs when TAF was given at the highest doses. There have not been cases of uveitis related to TAF in clinical studies, however, during this study you should immediately report any visual disturbances or eye pain you experience to your doctor and be evaluated.

TAF is a drug similar to Tenofovir disoproxil fumarate (TDF), Viread®, an approved medication by the FDA for the treatment of HIV and hepatitis B infection. Although the side effects for TAF are not known yet, the adverse effects are expected to be similar to Viread. The side effects for Viread® are listed below.

Tenofovir DF (TDF, Viread®)

Tenofovir DF has been studied in approximately 12,000 HIV-infected adults for as long as 480 weeks in some patients. Common potential side effects identified in patients who received at least one dose of tenofovir DF 300 mg include diarrhea, nausea, vomiting, flatulence (intestinal gas), and dizziness. Those side effects were often mild or moderate in severity, and did not lead to discontinuation of tenofovir DF.

In addition to side effects reported from clinical trials the following side effects have also been identified after tenofovir DF was approved in HIV-infected patients treated with combination therapy that has included tenofovir DF and other anti-HIV drugs: weakness, abdominal pain, allergic reaction including potentially serious swelling of the face, lips, and/or tongue, with or without rash, pancreatitis (inflammation of the pancreas), high levels of amylase in the blood, shortness of breath, rash, abnormalities of tests that measure hepatic (liver) function and hepatitis (inflammation of liver).

Cases of lactic acidosis (high levels of lactic acid in the blood), liver problems with enlargement of the liver and fat in the liver, including fatal cases, were reported in HIV-infected patients treated with anti-retroviral agents similar to tenofovir DF. The symptoms of lactic acidosis include: weakness, unexpected and uncommon abdominal pain, nausea and vomiting. Symptoms of liver problems include yellowing of the skin or whites of the eyes, dark urine, light colored bowel movements, loss of appetite, nausea and lower abdominal pain. If you notice any of these symptoms, please request medical assistance immediately.

Cases of kidney damage have been reported in patients taking tenofovir DF who already have circulatory disease or specific kidney disease, and patients who, while receiving tenofovir DF, were also taking medications that may cause damage to the kidneys. Kidney damage has also been reported in patients without any of these factors. For example, some patients have had damage to the structure and function of the kidneys, which may lead to muscle abnormalities, muscular weakness, destruction of muscle tissue, bone pain and fractures due to softening of bones, and low potassium and phosphate in the blood. In addition, death of kidney tissue, continuous or sudden kidney failure, abnormal kidney function, inflammation of the kidneys, protein in the urine, excessive urination, nephrogenic diabetes insipidus (excretion of urine resulting in dehydration and thirst), and increased creatinine in the blood have also been reported in patients taking tenofovir DF. The approved dosing interval for tenofovir DF in patients with kidney function (glomerular filtration) below 50 mL/min is every 48 hours; in this study, you will be instructed to take the new form of tenofovir (tenofovir alafenamide) every 24 hours.

Bone toxicity, including a decrease in bone mineral density, was seen in animals following treatment with tenofovir DF. Decreases in bone mineral density have been seen in humans. The risk of bone fractures associated with these types of changes is unknown. One of the purposes of this study is to evaluate bone health using DEXA scans. Because reports of bone fractures have not been collected systematically, it is not possible to determine the rates at which these events happen.

If you are infected with hepatitis B virus (HBV), there is a possibility of an unexpected worsening of hepatitis B if you stop taking tenofovir DF.

Please talk to your study doctor for more details on side effects or refer to the tenofovir DF package insert for additional information.

Emtricitabine (FTC, Emtriva®)

The most common adverse reactions seen in at least than 10% of patients treated with FTC include headache, diarrhea, nausea, fatigue, dizziness, depression, trouble sleeping, abnormal dreams, rash, abdominal pain, weakness, increased cough and runny nose. The most common side effects seen in more than 10% of patients treated with FTC in combination with other anti-HIV drugs are headache, diarrhea, nausea, and rash.

Other common side effects seen more than 1% and less than 10% with emtricitabine include: vomiting, indigestion, changes in skin color primarily on the palms and/or soles, increased triglycerides (a type of fat in the blood), increased bilirubin in the blood (an indication of possible liver damage), increased sugar in the blood, allergic reaction, increased liver enzymes in the blood (an indication of possible liver damage), increased pancreatic enzymes in the blood (an indication of possible damage to the pancreas) and low white blood cell count. A reduction in your white blood cell count can make you more prone to infection. You may also experience muscle pain and increased muscle enzymes in the blood (an indication of possible muscle damage).

A serious condition called lactic acidosis (high levels of lactic acid in the blood), liver problems with enlargement of the liver and fat in the liver, including deaths were reported in HIV-infected patients treated with anti-HIV medications similar to emtricitabine. Symptoms of liver problems include yellowing of the skin or whites of the eyes, dark urine, light-colored bowel movements, and loss of appetite, nausea and lower stomach pain. If you notice any of these symptoms, you must immediately report them to the study doctor or staff.

If your kidney function (glomerular filtration) is reduced below 50 mL/min, the approved dosing interval for emtricitabine is every 48 hours; in this study, you will be instructed to take emtricitabine every 24 hours. In this circumstance, the drug levels of emtricitabine are likely to be higher, possibly increasing the risk of developing side effects associated with emtricitabine.

Switching from a stable regimen

If you are currently taking medications that are effectively treating your HIV infection, you will be changing your medication regimen from a stable regimen that is working well to a new regimen during this study. When switching from one antiviral regimen to another, there is a risk that the virus will not be controlled with the new regimen, that the virus could develop resistance to the medications, and that the new regimen could cause new side effects. Viral load, possible resistance, and side effects will be frequently and carefully monitored during this study to minimize these risks.

Immune Reconstitution Syndrome

A condition called immune reconstitution syndrome can happen in some patients with advanced HIV infection (AIDS) when combination anti-HIV treatment is started. Signs and symptoms of inflammation from opportunistic infection that a person has or had may occur as the medicines work to control the HIV infection and strengthen immune system.

Autoimmune disorders such as Graves' disease (a disease in which the thyroid produces excessive thyroid hormones), polymyositis (a disease of caused by inflammation leading to weakness of the muscles), and Guillain-Barre syndrome (a disease that occurs when the body's immune system attacks part of the nervous system, leading to nerve inflammation that causes muscle weakness), have also been reported to occur in the setting of immune reconstitution, however, the time to onset is variable and can occur many months after starting treatment. Call your study doctor right away if you notice any signs or symptoms of an infection after starting study medication.

Allergic Reaction Risks

As with taking any drug, there is a risk of allergic reaction. If you have a very serious allergic reaction, you may be at risk of death. Some symptoms of allergic reactions are:

- Rash
- Difficulty breathing
- Wheezing
- Sudden drop in blood pressure
- Swelling around the mouth, throat or eyes
- A fast pulse
- Sweating

Please seek treatment and alert the study doctor and study staff immediately if you have any of these symptoms, or any other side effects, during the study.

BLOOD DRAWS

Drawing blood from a vein may cause local pain, bruising, occasional lightheadedness, fainting, and very rarely, infection at the site of the blood draw.

ECG

After you have an ECG, you may have mild irritation, slight redness, and itching at the places on your skin where the recording patches are placed. You may have to have your chest shaved for this procedure.

DEXA

Decreases in bone mineral density have been observed in HIV-infected patients. An X-Ray called dual energy X-ray absorptiometry, or a DEXA scan, will be performed on your spine and hip to measure changes in bone mineral density.

DEXA scan will be performed at the Day 1 (baseline) visit, Weeks 24, 48, 72, and 96.

DEXA scans involve exposure to radiation. Therefore, you will receive a radiation dose. This radiation dose is not necessary for your medical care and will occur only as a result of your participation in the study. At doses much higher than you will receive, radiation is known to increase the risk of developing cancer after many years. At the doses you will receive, it is very likely that you will see no effects at all.

Hepatitis B and C Testing Risks

At the Screening visit, you will be tested for hepatitis B and C, and the results of these tests will be reported to the PA Department of Health. You will be told, face-to-face, the results of these tests. Counseling will be available to you if necessary.

Renal Sonogram

You will have a renal sonogram (kidney ultrasound) at your Baseline visit. The technician, or sonographer, will use a small amount of water-based, non-irritating gel that allows the transducer to glide smoothly on your skin. The gel creates a cool sensation on your skin and the transducer's movement creates light pressure, but you should feel no discomfort during the test. There is no radiation used in this test.

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UNKNOWN/UNEXPECTED RISKS AND DISCOMFORTS

In addition to the risks listed above, there are risks that are not known or do not happen often when subjects take these study drugs, including severe or life-threatening allergic reactions, interactions between study drugs or interactions with another medication. You will be informed in a timely manner, both verbally and in writing of any new information, findings or changes to the way the research will be done that might influence your willingness to continue to take part in this study.

PREGNANCY AND BREAST-FEEDING

The effects of TAF and TDF have not been fully evaluated on the developing fetus in humans. Animal studies do not indicate direct or indirect harmful effects of TAF and TDF with respect to pregnancy. Because the effects of TAF and TDF on a developing fetus as well as on exposed infants are unknown, any female able to become pregnant (i.e., A female subject of childbearing potential is a nonmenopausal female who has not had a hysterectomy, bilateral oophorectomy, or medically documented ovarian failure. This definition includes a young woman who has not yet started menstruating) must have a negative blood pregnancy test to enroll; females who are breast-feeding will not be enrolled in this study.

It is very important while you are in this study that you do not become pregnant if you are a female, or do not cause others to become pregnant if you are a male. Not having sex is the only certain way to prevent pregnancy.

If you are a sexually active male or female, it is required that you use a protocol recommended method of birth control from the screening visit throughout the study and for 30 days following the last dose of study drug.

Protocol-recommended contraceptive methods are: (1) a combination of one hormonal method and one barrier method; (2) two barrier methods where one method is the male condom ; or (3) use of an IUD or tubal sterilization (see table below). Acceptable hormonal methods include: injectable progesterone, progesterone implants, combination oral contraceptives, transdermal patch, and vaginal ring. If you are female and use hormonal contraceptives as one of your birth control methods you must have used the same method for at least 3 months before study drug dosing. Since the effect of the study drugs on hormonal contraceptives is unknown, if you are on hormonal contraceptives you must agree to a barrier method in addition to continuing your current hormonal contraceptives. Acceptable barrier methods include: diaphragm, cervical cap, and the male condom. If you are female, you must use either a hormonal method or a barrier method if the partner has a vasectomy.

Protocol-Recommended Contraceptive Methods

Methods to Use by Themselves	Combination Methods	
	Hormone Methods (choose one and use with a barrier method)	Barrier Methods (use both OR choose one and use with a hormone method)
Intra-uterine devices (IUDs) <ul style="list-style-type: none"> • Copper T 380A IUD • LNG 20 IUD 	Estrogen and Progesterone <ul style="list-style-type: none"> • Oral contraceptives • Transdermal patch • Vaginal ring Progesterone <ul style="list-style-type: none"> • Injection • Implant 	<ul style="list-style-type: none"> • Diaphragm OR <ul style="list-style-type: none"> • Cervical cap • Male condom
Tubal sterilization	Partner's vasectomy must be used along with a hormone or barrier method.	

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If you are a female who is sexually active and able to become pregnant, please speak with your study doctor to determine the best method of birth control for you to use during this study. Hormone-based contraceptives may not be effective at preventing pregnancy when they are used with study drug.

Even if you use a protocol recommended birth control method, you could still become pregnant. There is a slight chance that a pregnancy test could be wrong. If the pregnancy test is wrong, and you receive the study drug while pregnant, the study drug may harm an unborn baby.

If you are female and become pregnant or suspect that you have become pregnant while in the study and within 30 days of last dose of study drug, you will be required to stop taking all the study drugs and to notify your study doctor immediately. You will be discontinued from the study. The study doctor will request to track your pregnancy and will report the pregnancy and outcome (problems during pregnancy, health of the baby at delivery, ie. Weight, APGAR scores) to Gilead. This information will be obtained by asking you about your pregnancy and its outcome; if you cannot recall the information, we may ask you to sign a release form so that the information can be obtained from your hospital records or from your obstetrician.

Other not yet identified side effects could occur to you, your embryo or fetus should you become pregnant during the time you participate in the study or after you have completed the study.

CONDOM USE

It has been proven that condom use decreases the risk of spreading HIV and hepatitis B between sexually active individuals. To decrease your risk of transmitting the virus to another individual and to decrease the risk of being infected with a different strain of HIV, we recommend that condoms (except for lambskin) be used for all sexual activity to include oral, vaginal, and anal sexual contact. Condom use is recommended in addition to your current form of birth control. The use of spermicide is not recommended if you or your partner is HIV-infected. Male subjects must agree to use condoms during heterosexual intercourse and avoid sperm donations while enrolled in the study and for 30 days after administration of the last dose of study drug.

POSSIBLE BENEFITS OF THE STUDY

There is no guarantee that you will receive personal benefit from participating in this study. The study drugs are not expected to cure you of HIV. However, clinical research studies such as this are a way for doctors to determine if a drug is useful in fighting a disease. By taking part in this study, you and the Sponsor, Gilead Sciences, Inc., may benefit if E/C/F/TAF is effective in treating HIV-1 infection. Your participation in this study may benefit the community, scientists and doctors who work with HIV by providing increased knowledge and information about the treatment of your disease. In addition, during your participation you will have close medical monitoring of your health condition by blood tests and other evaluations during clinic visits.

TREATMENT OPTIONS

You have the option to discuss with your study doctor not to have treatment or to choose other anti-HIV drugs to treat your disease. These medicines include commercially available medicines. Your study doctor will discuss appropriate alternative treatment options with you. You will be made aware of any new findings that become available during the course of the study that may affect your willingness to participate in this study.

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WITHDRAWAL FROM STUDY AND REFUSAL TO PARTICIPATE

Special care will need to be taken when determining if you need to stop the study drug. Your study doctor will supervise any discontinuation of the study drug with your health as the first priority. Your participation in this study may be stopped at any time by a) your study doctor, b) Gilead Sciences, Inc., c) the FDA, d) the Institutional Review Board (a review group that gives approval to your study doctor to conduct this study), and (e) other appropriate regulatory agencies.

Your participation in this research study is voluntary and you can refuse to participate or stop at any time without stating a reason. Your withdrawal will not affect your access to other medical care.

Your study doctor may withdraw you from the study if a change to your treatment regimen is required or if it is considered important for your medical safety. If it is learned that you did not give an accurate medical history or did not follow the instructions for the study given by your study doctor and/or study nurse, you may be taken off the study at any time. If you are taken off the study, you will no longer receive the study drugs.

COST OF TREATMENT

The study drug used in this study will be given to you free of charge. All clinic, professional, diagnostic, and laboratory fees for tests and procedures that are part of this study will be provided at no cost to you. You or your usual health care payer will be responsible for any other health care costs.

PAYMENT FOR PARTICIPATION

You will be paid \$25.00 for your screening visit. For visits thereafter, Baseline and 13 visits through wk 96 (1, 2, 4, 8, 12, 16, 24, 36, 48, 60, 72, 84, 96), you will be paid \$40 for every visit you attend. An additional payment of \$10 will be made at these visits if you bring back the study medication bottles dispensed at the last visit (empty or with any unused study drugs). For visits after Week 96, \$50 compensation will be provided. An additional compensation of \$25 will be provided for regular study visits that require a DEXA scan; there are 5 DEXA scans required (Baseline and one every 24 wks to week 96). Please note that if a separate visit is required to complete the DEXA scan, \$50 will be provided as compensation. Thus if you attend all required visits, complete the 5 DEXA scans and return your medication bottles for the study through wk 96, the maximum payment you can receive is \$850. If you stop taking study drugs early and complete the Early Study Drug Discontinuation Visit and return the study medication bottles, you will be compensated \$50. If a DEXA Scan is needed at this visit, additional compensation of \$25 will also be provided. You will be compensated \$50 for the 30-Day Follow-Up Visit that occurs after the Early Study Drugs Discontinuation Visit. You will be compensated \$25 for any unscheduled visits requested by the study staff. The total payment you will receive for the study depends on how long you participate.

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 an Individual Tax Identification Number or Social Security Number for tax purposes.

COMPENSATION FOR STUDY-RELATED INJURY

If you become sick or injured as a direct result of taking the study drug and/or following the study procedures, the University of Pennsylvania will provide you with medical treatment. The Sponsor, Gilead Sciences, Inc., will reimburse you or the University of Pennsylvania for the reasonable and necessary costs of such medical treatment. No other form of reimbursement for study-related injury or illness is offered by the Sponsor. You do not give up any legal rights by signing this form. You should immediately contact your Study Doctor at the contact information on page 1 of this form in the event you experience any study-related illness or injury.

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If you receive Medicare benefits, the Sponsor, Gilead Sciences, Inc., is required by law to report payments made to you for treatment, complications, and injuries that arise from this Study. Information that you are taking part in the Study, medical treatments received, Medicare claims, and other personal information about you such as your name, social security number, and date of birth, will be provided to the Centers of Medicare and Medicaid Services and its agents and/or contractors for this purpose.

STATEMENT ABOUT PRIVACY

Records identifying you will be kept confidential and, to the extent permitted by applicable laws and/or regulations, will not be made publicly available. Your personal information may be given out if required by law. If you test positive for HIV, Hepatitis B or Hepatitis C, by law we have to report the infection to the City of Philadelphia Health Department/PA Department of Health. We would report your name, gender, racial/ethnic background, and the month and year you were born. This is to keep track of how many people in the U.S. have HIV infection. It is also to make sure that states get enough money from the federal government to support the medical care of people living with HIV. The Health Department does not share the names of HIV infected people with anyone else. It removes all personal identifiers, such as your name, before giving information on the number of HIV infections to the federal government. Please note that it is likely that this information has been already reported to the PA Health Department as the HIV test being done for this study is not the first test for you. In the event of any publication regarding this study, your identity will remain confidential.

To further protect your confidentiality on the study, you will be assigned a code number. This code number will be used to label all your samples for testing and the information collected about you as part of your study visits will be entered into a database by this code number. Records that have your name and personal information will have restricted access and stored in locked cabinets in a secure facility.

Representatives from government agencies, including the U.S. Food and Drug Administration ("FDA"), institutional review boards, the Sponsor and/or the Sponsor's authorized representatives may need access to your original medical records and study records for the purpose of checking data collected for the study. By signing this consent form, you authorize this access.

Your coded study information and samples may also be used for additional unanticipated medical and/or scientific research projects in the future relating to HIV-1 or the development of the E/C/F/TAF (but at all times in compliance with applicable law and regulation).

AUTHORIZATION TO USE AND DISCLOSE RECORDS

The authorization part of the consent gives more detailed information about how your personal health information may be used and disclosed by the University of Pennsylvania Health System (UPHS), the School of Medicine and the individual Principal Investigator, subject to University of Pennsylvania procedures.

What personal health information is collected and used in this study and might also be disclosed?

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, date of birth
- Social Security Number (if you receive more than \$600 for participating in studies at PENN, we

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will need your SSN for the W-9); medical record number

- Personal and family medical history
- Current and past medications or therapies
- Results of physical exams, laboratory tests and procedures you will undergo during this research study

Why is your personal contact and health information being used?

Your personal contact information is important for the research team to contact you during the study. Your personal health information and results of tests and procedures are being collected as part of this research study. In some situations, your personal health information might be used to help guide your medical treatment.

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

The following individuals may use or disclose your personal health information for this research study:

- The Principal Investigator and the Investigator's study team
- Authorized members of the workforce of the UPHS and the School of Medicine, and University of Pennsylvania support offices, who may need to access your information in the performance of their duties (for example: for research oversight and monitoring, to provide treatment, to manage accounting or billing matters, etc.).

Who, outside of UPHS and the School of Medicine, might receive your personal health information?

As part of the study, the Principal Investigator, the study team and others listed above, may disclose your personal health information, including the results of the research study tests and procedures. This information may be disclosed to those listed below:

Individuals or organizations responsible for administering the study:

- Pharmaceutical sponsor (Gilead Sciences): This is the company that supplies drugs for the study. Information regarding safety and adverse effects needs to be collected and monitored.
- Contract Research Organization: Monitors will visit the site on a regular basis to review data and assure accuracy and completeness of information before the data are analyzed.
- BioClinica: This is the central reading facility that will review your DEXA scan for the sponsor. It is important that one team review all the scans for all of the participants for quality control purposes.

Regulatory and safety oversight organizations

- The Food and Drug Administration and regulatory agencies in other countries
- The Office of Human Research Protections
- The Study Monitoring Committee

Once your personal health information is disclosed to others outside of UPHS or the School of Medicine, it may no longer be covered by federal privacy protection regulations. Data are reported to the sponsor on Case Report Forms that identify you by your unique study number and not your name or medical record number. Information regarding your health, such as side effects of the study medications you experience will be reported only by code number. All samples collected for analysis will be labeled with your study number, visit number and date of your visit.

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The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

How long may UPHS and the School of Medicine be able to use or disclose your personal health information?

Your authorization for use of your personal health information for this specific study does not expire.

Your information may be held in a research repository (database). However, UPHS and the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization to do so
- The University of Pennsylvania's Institutional Review Board grants permission after ensuring that appropriate privacy safeguards are in place
- As permitted by law

Will you be able to access your records?

Since this is an open-label study, you will be able to access some or all of your medical records after the study is over. The Principal Investigator is not required to release research information to you that is not part of your medical record.

Can you change your mind?

Yes, at any time you may withdraw your approval to allow the use and disclosure of your personal health information as described here. You must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, your personal health information that was collected before we received your written request may still be used and disclosed, as necessary for the study. If you withdraw your permission to use your personal health information, you will also be withdrawn from the research study.

If you withdraw your permission to use any blood or tissue obtained for the study, the Sponsor may need to retain and use any samples that have already been collected to comply with its legal obligations and to maintain the scientific integrity of the study.

You will be given a copy of this Research Subject HIPAA Authorization describing your confidentiality and privacy rights for this study. You will also be given the UPHS and School of Medicine's Notice of Privacy Practices that contains more information about the privacy of your personal health information.

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

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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).

WHO CAN I CALL WITH QUESTIONS, COMPLAINTS OR IF I'M CONCERNED ABOUT MY RIGHTS AS A RESEARCH SUBJECT?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

RESEARCH STUDY REGISTRY

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

STORAGE AND USE OF URINE SAMPLES

A portion of the urine samples taken at each visit, except screening, will be frozen and stored. The stored urine samples may be used by the Sponsor or its research partners for possible additional clinical analyses. At the conclusion of this study, these samples may be retained in storage by Gilead Sciences, Inc. for a period up to 10 years.

STORAGE AND USE OF BLOOD SAMPLES

A portion of your blood sample drawn at each visit, except screening, will be frozen and stored. These stored blood samples and the information collected about you during the study may be used by the Study Sponsor or its research partners for HIV-1 genotyping/phenotyping assays or their development, for retesting the amount of HIV-1 in your blood, for measurement of antiviral drug levels in the blood, for future testing to learn more about how the study drug has worked against HIV-1 or clinical laboratory testing to provide additional clinical data. At the conclusion of this study, these samples may be retained in storage by Gilead Sciences, Inc. for a period up to 10 years.

Genotype testing detects changes or "mutations" in certain genetic regions of the HIV-1 virus. Phenotype testing is used to determine whether a mutation in an HIV-1 gene changes how anti-HIV drugs affect the HIV-1 virus. Some mutations can prevent certain anti-HIV drugs or drug regimens from reducing the level of HIV-1 in your blood. When this occurs, the HIV-1 has become "resistant" to that drug and possibly other similar drugs. Genotype and phenotype tests may be experimental;

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that is, these tests may not have been approved by the FDA. The results of such tests are for research use only, and the interpretation of the test results may not have direct benefit to you. At the conclusion of this study, these samples may be retained in storage by Gilead Sciences, Inc. for a period up to 10 years.

No human genetic testing will be performed without your expressed consent.

Blood Sample Storage for Future Research

As an optional part of this study, you are also being asked to allow the Study Sponsor to store your blood samples for future testing to learn more about how the study drug(s) has worked against HIV-1. From these samples, it might also be possible to learn more about what causes HIV-1, how to prevent HIV, or how to better treat HIV. These samples may be also be used for purposes that are not yet known.

If you choose to allow your samples to be banked for future research, about 14 mL (about 3 teaspoons) of blood will be drawn at all study visits (starting at Day 1) to be frozen and stored. If you do not agree to banking of your samples, you can still take part in the main research study.

You should also know that the Sponsor and other researchers who may study your blood samples have an economic interest in developing new drugs and medical tests. The results of this research may lead to a commercial product for the diagnosis, cure, mitigation, treatment, or prevention of disease. You understand and agree that by consenting to the storage of your samples for possible future research, you authorize the use of your sample, the by-products of the sample, and any products developed from the sample as described by this form. The Sponsor or other researchers or research companies may patent or sell discoveries that result from this research. Neither the Sponsor nor the Study Doctor has any plans to compensate you if this happens.

Withdrawing consent to the storage and future testing of your sample will result in destruction of your sample. However, if you withdraw your consent after the sample has been tested, the test results and research study/sample-related information must remain in any database(s) that were created for the research study. The reason for this is to comply with regulations that require the Sponsor to make data available for review by the United States Food and Drug Administration (FDA) or other appropriate regulatory authorities, or if this research is used to support an application for FDA approval to market the study drug.

If you withdraw consent for participation in the main study or are discontinued from the main study, the blood sample you provided will continue to be available for storage and future testing unless you also withdraw your consent for this purpose as stated above.

Please initial next to one of the statements below to indicate whether or not you agree to allow storage of your samples for possible future research outside of the main research study.

Yes_____ No_____ I agree to allow my blood samples to be stored for future research outside of the main research study.

