UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

Gilead Sciences, Inc. GS-US-337-0115, 25-NOV-2013

A Phase 3, Multicenter, Open-Label Study to Investigate the Efficacy and Safety of Sofosbuvir/Ledipasvir Fixed-Dose Combination for 12 Weeks in Subjects with Chronic Genotype 1 or 4 Hepatitis C Virus (HCV) and Human Immunodeficiency Virus (HIV)-1 Co-infection

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

Your contacts for this study are:

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

INTRODUCTION

You are being asked to take part in a clinical research study involving an investigational fixed dose combination (FDC) tablet called Sofosbuvir/Ledipasvir (SOF/LDV) FDC for the treatment of the Hepatitis C virus (HCV) in subjects who are co-infected with Human Immunodeficiency Virus (HIV).

This Informed Consent Form tells you about the study. Your Study Doctor or study nurse will go over this with you and answer any questions you may have regarding the study. Ask your Study Doctor or study nurse to explain any words or information in this consent form you do not clearly understand. You should understand the purpose of the study, how taking part may help you, any potential risks to you, and what is expected of you during the study.

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. If you agree to take part, you will be asked to sign and date this consent form and will be given a signed and dated copy to keep. No one can force you to take part in this study. Even if you agree to take part now, you can change your mind and stop at any time without penalty or loss of benefits to which you would otherwise have.

PURPOSE OF THE STUDY

The purpose of this study is to see if Sofosbuvir/Ledipasvir fixed-dose combination (SOF/LDV FDC) given for 12 weeks is safe and able to clear the Hepatitis C virus (HCV) from subjects who are co-infected with HIV-1. SOF/LDV FDC is an investigational drug. Investigational drugs are drugs that are not approved by the United States (US) Food and Drug Administration (FDA). Investigational drugs may be tested in research studies such as this one. The current standard of care for persons with HCV genotype 1 or 4 is Sovaldi™ (Sofosbuvir), pegylated interferon and RBV.

DESIGN OF THE STUDY

If you agree to take part in this study, you will be one of approximately 300 subjects at about 60 study sites in North America and New Zealand. About 5 people are expected to enroll at the University of Pennsylvania. This study is open to male and female subjects, at least 18 years of age, who have chronic genotype 1 or genotype 4 Hepatitis C virus infection, are co-infected with HIV-1 and who meet the study requirements. A"genotype" is the classification of a virus based on its RNA make up. The numbers 1-6 for HCV simply just refer to the numbers of distinct groups of virus that have been found so far.

Genotype 1 is the most common type in the US. The Study Doctor has asked you to come to the clinic for a screening visit to see if you are eligible to take part in the study.

This is an open-label study, which means that you and your study doctor will know exactly what medications you are taking. If you agree to take part in this study and meet all of the requirements you will take a SOF/LDV FDC tablet daily for 12 weeks.

The study drug Sofosbuvir 400 mg/Ledipasvir 90 mg FDC will be supplied by Gilead Sciences, Inc., which is also the sponsor of this study. The SOF/LDV FDC tablet should be taken by mouth once a day with or without food. You should never crush or split any of your study tablets. The study drug should be stored at room temperature (approximately 77˚ F). You should continue to take your HIV medications as prescribed while on this study.

DURATION OF THE STUDY

Your participation in this study will last up to 40 weeks. This study is made up of the following parts:

- Screening: Up to 28 days (or 42 days if you require a liver biopsy or additional Hepatitis C virus type testing); includes one visit to your Study Doctor lasting approximately 2 to 4 hours
- Study Treatment: 12 weeks of study drug treatment; includes 8 visits lasting 1 to 2 hours each
- Follow-Up: Up to 24 weeks of follow-up after your last dose of study drug; includes up to 3 visits lasting 1 to 2 hours each

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:

- You must be able to provide written consent to be in 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.
- You must tell your Study Doctor all of the medications that you have been taking for at least 30 days before you take part in the study. This includes vitamins, minerals and medications that do not require a doctor's prescription. Some medications are not allowed. Your Study Doctor will discuss these with you in detail.
- You must ask your Study Doctor before starting any new medications during the study.
- You must not become pregnant or get someone pregnant during this study.
- It is very important that you attend all visits as scheduled, including all of the follow-up visits.
- Only you should take the study drugs. They must be kept out of reach of children. Please also keep the study drugs away from people who may not be able to read or understand the label.
- You must return all of the used and unused study drug materials (including empty drug bottles) at every study visit.
- You must 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.

If you cannot follow these rules, you should not be in the study.

STUDY PROCEDURES

You will be receiving treatment for HCV as part of this study and the procedures below are done to monitor your safety and your response to the treatment. If you were getting treatment outside the study, some of tests would also be done. These tests will be shared with your provider (if you like) so that she or he can monitor your health as well. It is likely that no other labs will need to be done by your provider. Some samples collected would not be collected as part of routine care and are only be collected for the study. A description of all procedures performed at each visit appears below:

Screening

Your Study Doctor will do some tests or procedures (described below) to see if you meet the requirements for being in the study. The following procedures will be done at the screening visit(s), which will last approximately 2 to 4 hours.

- You will discuss and have time to review this consent form in detail and you will have time to have all of your questions answered. You will be asked to give informed consent by signing and dating this form.
- You will be asked questions about your Hepatitis C, HIV and medical history (including prior and current Hepatitis C and HIV treatments).
- You will be asked about any medications you are taking or have taken within the last 30 days.
- You will have a physical exam, including measurement of your height, weight, and vital signs (blood pressure, heart rate, breathing rate, and temperature).
- You will have an ECG (or "electrocardiogram", which is a recording of the electrical activity of your heart).
- Blood samples will be taken by a needle stick into a vein in your arm. During the entire study, approximately 600 mL (approximately 40 Tablespoons) During the screening visit approximately 49 ml (3.5 Tablespoons of blood will be collected. of blood will be taken. Your blood will be collected for:
    - Safety tests (to check how your liver, muscles, kidney, blood cells and other body systems are working)
    - Hepatitis C virus (the type and amount of virus in your blood)
    - HIV (the virus that causes AIDS)
    - CD4 T cells count (white blood cells that fights infection)
    - Hepatitis B virus
    - Thyroid tests (hormones made by a gland in your neck)
    - Coagulation tests (to check the ability of your blood to clot)
    - IL28B genotype test (to obtain information on the potential ability to respond to treatment, see "Genetic Testing" section below)
    - Pregnancy (if you are a woman who could become pregnant)
- Urine will be collected for safety tests and to see how your kidneys are working. In addition, your urine will be screened for drugs to determine if you have recently used methadone, amphetamines, cocaine and/or opiates. If this drug screen is positive, you will not be eligible to participate in this study unless it can be explained as a prescribed medication by your Study Doctor.
- It will be determined whether or not you have cirrhosis (liver damage) by a blood test. You may also need a Fibroscan (an ultrasound of your liver) or a liver biopsy to determine if you have cirrhosis. These evaluations are necessary to see if you qualify for the study and are done solely for the study (as part of your regular clinical care you may not need to have the biopsy done in order to get treatment).

The Fibroscan or liver biopsy may be done in a hospital or other clinic. If a liver biopsy is necessary, your doctor will provide you information about these tests and may obtain your permission with a separate hospital or clinic consent form. No additional specimens from the biopsy would be collected or stored by the study; only the amount of tissue needed to perform the test for cirrhosis would be taken.

Genetic Testing

As part of this study, we will take a separate sample of your blood during screening to test a small piece of DNA (IL28B) that has been shown to predict who is most likely to respond to Hepatitis C treatment with interferon-based treatments. It is unknown whether this gene is important in predicting your response to the investigational treatment you may receive in this study.

If you do not allow this particular genetic test (IL28B genotype) to be done, you may not participate in this study. Your blood samples will not be used for any other genetic or DNA testing without separate consent.

If you cannot perform or do not want to do any of these procedures, you should not agree to be in this study.

Your Study Doctor will look at the results of your screening tests to see if you qualify for the study. If your Study Doctor finds you eligible to take part in the study and you agree to continue, a "Baseline" (1st day of taking study drug) visit will be scheduled within 28 days of the screening visit (or within 42 days if a liver biopsy or additional Hepatitis C virus type testing is needed).

Study Treatment

Baseline (1st day of taking study drug)

The Baseline visit will include the following procedures and will last approximately 1 to 2 hours:

- Your Study Doctor will review the study entrance criteria to see if you are still able to participate
- You will have a physical exam, including measurement of your weight, and vital signs (temperature, blood pressure, heart rate, and breathing rate)
- You will also be asked if you have taken any medications including any non-prescription (over-the-counter) medications since your last study visit, as well as any changes in your health (illnesses or health problems) you have experienced since your last study visit.
- You will have an ECG (or "electrocardiogram")
- You will be counselled on pregnancy prevention
- Samples of your blood 55ml (approximately 4 Tablespoons) will be collected for:
    - Safety tests (to check how your liver, muscles, kidney, blood cells and other body systems are working)
    - Various HCV tests:
        - Review of the amount of virus in your blood.
        - Viral sequencing of the Hepatitis C virus in your blood
    - Various HIV tests:
        - Review of the amount of virus in your blood
        - Viral sequencing of the HIV in your blood
    - CD4 T cell count (white blood cell that fights infection)

  - Pharmacokinetics (blood samples to measure the amount of study drug in your body)
  - Coagulation tests to measure the ability of your blood to clot
- Optional blood sample for storage. If you choose to have blood samples drawn for storage, you will have the blood drawn at this visit. If you agree, an extra12 mL (approximately 1 Tablespoon) will be drawn.
- Optional blood sample for Pharmacogenomic testing (if the Pharmacogenomic Substudy informed consent form was signed). If you agree an extra 6 mL (approximately 1 teaspoon) will be drawn Pharmacogenomic testing can help understand markers of health and disease and why some people might benefit from the study treatment while others might not.
- Urine will be collected for safety tests and to see how your kidneys are working. **You will need to "fast" before this urine collection.** "Fasting" means no food or liquids (except for water) for at least 8 hours before your urine is collected. If you are not able to fast for this urine collection, you may return to the clinic sometime within 72 hours for this "fasting" urine collection.
- You will have a urine pregnancy test, if you are a woman who could become pregnant
- You will be asked to complete four quality of life questionnaires. These forms ask questions about your health, activities, and emotional well-being. The purpose of the questionnaires is to help us better understand how HIV/HCV co-infection affects your daily life. It should take you about 30 minutes to complete all of the surveys. You will read the questionnaires yourself and write or mark answers directly onto the questionnaires.
- If you still meet all the study requirements, you will be asked to take the first dose of study drug in the Study Doctor's office. You will be given instructions on how to take the study drugs at home.

Study Treatment Phase

The study treatment will last for 12 weeks. Study treatment visits are scheduled at the end of weeks 1, 2, 4, 6, 8, 10, and 12. The study staff will instruct you when to return for your next visit per the study plan.

The following will occur at every visit during study treatment:

- Measurement of your weight and your vital signs (temperature, blood pressure, heart rate, and breathing rate)
- You will also be asked if you have taken any medications including any non-prescription (over-the-counter) medications, other than the study drug, since your last study visit, as well as any changes in your health (illnesses or health problems) you have experienced since your last study visit
- You must bring all study drug(s) (including empty bottles) and all study material with you. The study staff will count how many tablets you have taken. You will be asked about any missed doses since your last visit. The study staff will give you a new bottle of study drug(s) to take home at weeks 4 and 8.
- Samples of your blood will be collected for: You will have between 35 and 73 mL (2.5 to 5 Tablespoons) of blood drawn depending on which study visit week you are attending.
  - Safety tests (to check how your liver, muscles, kidney, blood cells and other body systems are working)
  - Various HCV tests:
    - Review of the amount of virus in your blood.
    - Viral sequencing of the Hepatitis C virus in your blood.
  - Various HIV tests (at weeks 4, 8, and 12):

    - Review of the amount of virus in your blood.
    - Viral sequencing of the HIV in your blood
  - CD4 T cell count (white blood cell that fights infection) at weeks 4, 8 and 12
  - Pharmacokinetics (blood samples to measure the amount of study drug in your body)
  - Coagulation test, at week 12, to measure the ability of your blood to clot
- Optional blood sample for storage at week 12 (if you choose to have blood samples drawn for storage) If you agree, an extra12 mL (approximately 1 Tablespoon)
- Urine will be collected at each visit for safety tests and to see how your kidneys are working. **You will need to "fast" before this urine collection at weeks 2, 4 and 12.** "Fasting" means no food or liquids (except for water) for at least 8 hours before your urine is collected. If you are not able to fast for this urine collection, you may return to the clinic sometime within 72 hours for this "fasting" urine collection.
- You will have a urine pregnancy test every 4 weeks, if you are a woman who could become pregnant
- You will be counselled on pregnancy prevention at week 12
- You will be asked to complete four quality of life questionnaires at weeks 4. 8 and 12. These forms ask questions about your health, activities, and emotional well-being. The purpose of the questionnaires is to help us better understand how HIV/HCV co-infection affects your daily life. It should take you about 30 minutes to complete all of the surveys. You will read the questionnaires yourself and write or mark answers directly onto the questionnaires.
- Optional PK substudy: At either Week 2, 4, 6 **OR** 8 visit, blood will be drawn at multiple intervals to measure the amount of drug in your blood. You will need to sign a separate consent for this study. The University of Pennsylvania is participating in this substudy and all persons enrolled in the main study are eligible to participate until the study reaches its accrual goal.

You may be asked by your Study Doctor to stop taking the study drug earlier than scheduled if the amount of HCV in your blood remains at high levels, increases past a certain level, or you do not clear HCV from your blood – all of these events would suggest that the study drug was not effective for you. You will be asked to return for the Early Termination Visit and the follow-up visits (described below).

Early Termination Visit

If you stop treatment early, for whatever reason, you will need to have an Early Termination Visit to return your study medications and be checked by your doctor. The following procedures will occur at this visit:

- You will have a physical exam, including measurement of your weight, and vital signs (temperature, blood pressure, heart rate, and breathing rate)
- You will also be asked if you have taken any medications including any non-prescription (over-the-counter) medications, other than the study drug, since your last study visit, as well as any changes in your health (illnesses or health problems) you have experienced since your last study visit.
- All of your study drug bottles must be returned to your Study Doctor/staff at this time. The study staff will count how many tablets you have taken. You will be asked about any missed doses since your last visit.
- Samples of your blood 71 mL (approximately 5 Tablespoons) will be collected for
  - Safety tests (to check how your liver, muscles, kidney, blood cells and other body systems are working)
  - Various HCV tests:

        - Review of the amount of virus in your blood.
        - Viral sequencing of the Hepatitis C virus in your blood.
    - Various HIV tests:
        - Review of the amount of virus in your blood.
        - Viral sequencing of the HIV in your blood
    - CD4 T cell count (white blood cell that fights infection)
    - Pharmacokinetics (blood samples to measure the amount of study drug in your body)
    - Coagulation tests to measure the ability of your blood to clot
- Optional blood sample for storage (if you choose to have blood samples an extra12 mL (approximately 1 Tablespoon). drawn for storage)
- Urine will be collected for safety tests and to see how your kidneys are working. **You will need to "fast" before this urine collection.** "Fasting" means no food or liquids (except for water) for at least 8 hours before your urine is collected. If you are not able to fast for this urine collection, you may return to the clinic sometime within 72 hours for this "fasting" urine collection.
- You will have a urine pregnancy test, if you are a woman who could become pregnant
- You will be counselled on pregnancy prevention
- You will be asked to complete four quality of life questionnaires. These forms ask questions about your health, activities, and emotional well-being. The purpose of the questionnaires is to help us better understand how HIV/HCV co-infection affects your daily life. It should take you about 30 minutes to complete all of the surveys. You will read the questionnaires yourself and write or mark answers directly onto the questionnaires.

Follow-Up:

You will return to the clinic for follow-up visits starting 4 weeks after your last dose of study drug, even if you do not complete the treatment period as planned. The follow-up visits will be scheduled 4 weeks (1 month), 12 weeks (3 months), and 24 weeks (6 months) after your last dose of study drug. Each visit will last about 1 to 2 hours. You will have between 23 and 45 mL (1.5 to 3Tablespoons) of blood drawn depending on which study visit week you are attending

The following procedures will occur at the follow-up visits:

- Measurement of your weight and your vital signs (temperature, blood pressure, heart rate, and breathing rate)
- You will also be asked if you have taken any medications including any non-prescription (over-the-counter) medications since your last study visit, as well as any changes in your health (illnesses or health problems) you have experienced since your last study visit (follow-up week 4 only)
- Samples of your blood will be collected for:
    - Safety tests (to check how your liver, muscles, kidney, blood cells and other body systems are working)
    - Various HCV tests:
        - Review of the amount of virus in your blood.
        - Viral sequencing of the Hepatitis C virus in your blood.
    - Various HIV tests (at follow-up week 4 only):
        - Review of the amount of virus in your blood.
        - Viral sequencing of the HIV in your blood
    - CD4 T cell count (white blood cell that fights infection) at follow-up week 4 only

- Urine will be collected at each visit for safety tests and to see how your kidneys are working. **You will need to "fast" before this urine collection at follow-up weeks 4, 12 and 24.** "Fasting" means no food or liquids (except for water) for at least 8 hours before your urine is collected. If you are not able to fast for this urine collection, you may return to the clinic sometime within 72 hours for this "fasting" urine collection.
- You will have a urine pregnancy test at follow-up week 4, if you are a woman who could become pregnant
- You will be asked to complete four quality of life questionnaires at follow-up visit week 4. These forms ask questions about your health, activities, and emotional well-being. The purpose of the questionnaires is to help us better understand how HIV/HCV co-infection affects your daily life. It should take you about 30 minutes to complete all of the surveys. You will read the questionnaires yourself and write or mark answers directly onto the questionnaires.

If there is confirmed detectable HCV virus in your blood at any of the follow-up visits, you may be eligible to participate in a Retreatment Substudy. If you are eligible to participate in the Retreatment Substudy, your Study Doctor will discuss this with you. If you decide to participate in this Retreatment Substudy you will receive SOF/LDV FDC and Ribavirin for 24 weeks. After the 24 weeks of this retreatment, you will then complete a Retreatment Follow-up phase. During this follow-up phase, you will be required to attend visits 4 weeks, 12 weeks and 24 weeks after the last dose of treatment. You will be asked to sign a separate consent form which describes the Retreatment Substudy.

After all the Post-Treatment visits have been completed, you are done with this study.
If the Hepatitis C virus is clear from your blood by the end of the study, the Sponsor is interested in following your HCV status for up to 3 years after you stop taking study drug. Once you complete the Post-Treatment Follow-up Phase, you will be asked to sign a separate consent form for a different study to take part in long-term follow-up visits if this applies to you, called the SVR Registry.

If the Hepatitis C virus is not clear from your blood by the end of the study, the Sponsor is interested in following your HCV viral sequence for up to 3 years. Once you complete the Post-Treatment Follow-up Phase, you will be asked to sign a separate consent form for a different study to take part in long-term follow-up visits if this applies to you, called the Sequence Registry.

COLLECTION, STORAGE AND USE OF BLOOD SAMPLES FOR MAIN STUDY AND SUBSTUDIES
a) PK Substudy- Extra optional samples will be obtained and any leftover will be stored.
b) PG ssubstudy- One optional extra sample will be obtained and
c) Automatic storage of leftover samples obtained for main and retreatment studies for purposes related to this study- This is required and there is no separate choice related to this.
d) Optional storage of leftover samples obtained for main study for future research not related to this study. You will need to give your permission for this and will be asked to sign on page 20 of this consent.
e) **Additional blood sample collection for storage (optional):**
As an optional part of this research study, you will be asked if you will give two extra blood samples (1 tablespoon each day) during Baseline/Day 1 prior to first dose and at the Early Termination or Week 12 visit. These will be tested to see if there is a special kind of non-genetic marker in your blood that may identify those people who have a better response and/or outcome to treatment than others.

Study Procedures

	Screening	Baseline/Day 1	Study Visit Week								Post-Treatment Phase Week		
			1	2	4	6	8	10	12	Early Termination	4	12	24
Informed Consent	X												
Determine Eligibility	X	X											
Medical History	X												
Physical Examination	X	X							X	X			
Height & Weight[a]	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital Signs	X	X	X	X	X	X	X	X	X	X	X	X	X
ECG	X	X											
Adverse Events and Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X		
Pregnancy Prevention Counseling		X							X	X			
Health Related Quality of Life Surveys		X			X		X		X	X	X		
Assess Study Medication Compliance/ Pill Count			X	X	X	X	X	X	X	X			
Receive Study Drugs		X			X		X						
Blood and Urine Testing	X	X	X	X	X	X	X	X	X	X	X	X	X
Sample for Optional future research[b]		X							X	X			
PK substudy collection[c]				X	X	X	X						
Pharmacogenomic[d]		X											

a Height is only measured at the Screening Visit

b Only for subjects who agree to this extra sample

c Optional PK substudy. Will need to sign separate consent

d Only for subjects who have consented to this testing. If not obtained at Baseline/Day, the sample may be drawn at any time during the study.

RISKS

Your condition may or may not improve and could even get worse if you take part in this study. The Study Doctor and study staff will monitor you for any signs of new or unexpected side effects. Please tell your Study Doctor if you have a side effect or feel unwell while in this study. Contact your Study Doctor immediately if you experience a side effect that concerns you or are unable to perform your daily functions.

Common Side Effects for the Fixed-Dose Combination of Sofosbuvir and Ledipasvir (SOF/LDV)

The safety profile of SOF/LDV is based on the combined safety information from 3 large Phase 3 clinical studies in which SOF/LDV with and without ribavirin (RBV) was given to over 1900 HCV infected patients. In these studies, sofosbuvir 400 mg and ledipasvir 90 mg as a single fixed-dose combination tablet was given with or without RBV (up to 1200 mg per day) for 8, 12, or 24 weeks.

The most common side effects (≥ 10%) reported when SOF/LDV was given to 1080 patients were:

- Fatigue (tiredness) (22%)
- Headache (21%)
- Nausea (10%)

Most of the side effects were considered to be mild. Less than 1 in 100 patients had to stop taking SOF/LDV early because of a side effect.

Rare, but serious side effect:

- One HCV-infected person with hemophilia A (a bleeding disorder) who was taking SOF/LDV for 24 weeks, developed an antibody to Factor VIII, a protein that is important in preventing or stopping a bleed. It is unclear whether the development of this Factor VIII inhibitor was because the person had taken SOF/LDV, or was instead due to receiving factor VIII treatment, which hemophiliacs sometimes receive because of low levels of factor VIII.

It is not expected that you will have all of these side effects. Other side effects may occur that are not listed here or were not seen before. Please speak to your study doctor for more information. Side effects are usually temporary and can often be treated. However, it is very important that you report all side effects to your doctor as it is possible that side effects may suggest a serious or fatal health problem.

Other Adverse Events

Allergic Reaction

Occasionally, people have allergic reactions (including life-threatening reactions) when taking any medication. Symptoms of any allergic reaction can include rash, hives, itching and/or trouble breathing, closing of the throat, swelling of the lips, tongue or face, and rarely death. Immediately get emergency medical care if you have any of these symptoms. Stop taking your study drugs and let your Study Doctor know.

In general, allergic reactions to medicines are more likely to occur in people who already have allergies. If you are allergic to other drugs, foods, or things in the environment, such as dust or grass, you should let your Study Doctor know. Also, if you have asthma, let your Study Doctor know.

Blood Drawing Risks

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 Risks

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 need your chest shaved for this procedure.

Liver Biopsy Risks

Liver biopsy may be used to confirm the diagnosis of chronic Hepatitis and cirrhosis. Many doctors also do a liver biopsy to help confirm cirrhosis, how seriously the liver is damaged. Risks and complications of liver biopsy may include:

- Pain and discomfort located at or near the puncture site and radiating upwards toward the right shoulder region
- Bleeding at the biopsy site
- Possible internal bleeding for up to a few hours after the procedure
- Infections at the biopsy site or internal organs
- Puncture of internal organs (gall bladder, lung, intestine or kidney)
- Allergic reaction to the anesthetic

The risks and complications of liver biopsy mentioned above is by no means a complete list. Your Study Doctor will discuss all the risks and complications of the biopsy with you. You will be asked to read, understand and sign a separate consent for a liver biopsy.

Viral Resistance

Treatment with drugs that directly inhibit the Hepatitis C virus has been shown to lead to development of Hepatitis C virus that is resistant to that drug and other drugs with the same type of action. These resistance mutations have been observed in the body as late as 4 to 5 years after treatment has ended. It is unknown whether having these resistance mutations might reduce the chance of treatment success with future drugs with the same type of action or with different types of action (such as protease inhibitors). It is possible that if you are treated with the drugs in this study and treatment doesn't work, you might have resistance mutations that would make future treatment less successful.

Unknown Risks

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

Because the effects of SOF and LDV on an unborn baby (fetus) or a nursing infant are not known, any female who is pregnant or breast feeding an infant will not be enrolled in this study.

For subjects taking SOF/LDV FDC, extreme care must be taken to avoid pregnancy in female subjects or in female partners of male subjects during this study and following completion of study treatment (30 days after completion for women, 90 days after completion for men).

If you are a woman who is pregnant or a female with the intent of becoming pregnant or a female who is currently nursing (breastfeeding) a child, you cannot be in this study. If you are a man whose partner is currently pregnant or wishing to become pregnant, you cannot be in this study.

You must protect yourself or your partner from becoming pregnant before, during, and after the study. Women, and men with female partners capable of becoming pregnant, must use effective methods of birth control as described below. Your Study Doctor will need to document what type(s) of birth control you are using.

Women only:

Women who can get pregnant should not take study drug(s) unless they and their partner do not have intercourse ever or are using 2 methods of birth control for the duration of the study (starting 3 weeks prior to the Baseline/Day 1 visit) and for a minimum of 30 days after last dose of study drug or longer as directed by your Study Doctor.

At least one method of birth control must be a condom used correctly by your male partner. Your Study Doctor will discuss with you other methods of birth control that can be used in combination with a condom. Possible options of birth control to be used with condoms are: a) intrauterine device (IUD) with a failure rate of < 1% per year; b) female barrier method: cervical cap or diaphragm with spermicidal agent c) tubal sterilization; d) vasectomy in male partner; e) hormone-containing contraceptive: i) implants of levonorgestrel, ii) injectable progesterone, iii) oral contraceptives (either combined or progesterone only), iv) contraceptive vaginal ring v) transdermal contraceptive patch

Women who can get pregnant must have a negative pregnancy test at screening and at the Baseline/Day 1 visit, prior to taking the first dose of study medication. Pregnancy tests will be repeated every 4 weeks during the study treatment through the Post-Treatment week 4 follow up visit.

You must tell your Study Doctor immediately if you become pregnant while in this study and for a minimum of 30 days after stopping study drugs, or for as long as you have been directed by your Study Doctor to use contraception. The Study Doctor will tell you about the possible risks to your unborn child and options available to you.

In the event of a positive urine pregnancy result, you will be instructed to stop study drugs immediately and return to the study clinic as soon as possible for a serum (blood) pregnancy test. The pregnancy will be followed to its completion and the outcome, including any premature termination, must be reported to the Sponsor.

You should be counselled and monitored by your own doctor. As the risk to the unborn baby is unknown, it is recommended you seek medical supervision from your own doctor during the pregnancy and for the baby after it is born. Neither the study Sponsor nor the Study Doctor will be responsible for providing routine medical care relating to the pregnancy.

Men only:

If you have a female partner who cannot become pregnant, you must still consistently and correctly use a condom.

If you have a female partner who can become pregnant, you and your partner must use two forms of birth control for the entire study and for a minimum of 90 days after the last dose of study drug or longer as directed by your Study Doctor. You must use a condom while your female partner uses 1 other method of birth control (see above). Your Study Doctor will discuss with you other methods of birth control that can be used in combination with a condom.

If your female sex partner becomes pregnant while you are in the study or within 90 days after your last dose of study drug, the study drug may harm an unborn baby. If you have a female partner who becomes pregnant or suspects that she has become pregnant while you are in the study or within 90 days after your last dose of study drug, you will be required to notify your Study Doctor immediately. As the risk to your partner and unborn baby are not known, it is recommended for your partner to receive appropriate prenatal care. If you agree, your partner will be asked to sign a consent form to allow

disclosure of medical information related to pregnancy. Your Study Doctor may need to disclose to your partner details of this study and your taking part in it. The Study Sponsor and the Study Doctor will not be responsible for the costs related to the pregnancy, delivery, or care of your child.

Male subjects must also agree not to donate sperm from the time you take your first dose of study medication until 90 days after the last dose of study drug.

Please note: Hormonal birth control may be more effective when taken for at least 3 months. Even if you and your female partner use a medically proven birth control method, you could still cause your partner to become pregnant.

Please share this information with your partner.

POSSIBLE BENEFITS OF THE STUDY

There is no guarantee that you will receive personal benefit from taking part in this study. The study drug SOF/LDV FDC may not improve your chronic HCV. There is the possibility that your chronic HCV and HIV may worsen. 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 SOF/LDV FDC is effective in treating HCV/HIV co-infection. Your taking part in this study may benefit the community, scientists, and doctors who work with HCV and HIV by providing increased knowledge and information about the treatment of your disease. By taking part in this study, you will have close medical monitoring of your health condition by blood tests and other evaluations during clinic visits.

TREATMENT OPTIONS

You should ask your Study Doctor about all the treatment options that are available for treatment of HCV and HIV including approved and other investigational medicines. You should discuss with your Study Doctor whether you should receive treatment for your HCV and HIV now or wait longer to begin treatment. It is possible that other therapies for HCV may become available during your involvement in the study so it may be in your best interest to wait. Your Study Doctor will discuss all of your treatment options with you. You will be made aware of any new findings during the course of the study that may affect your willingness to participate.

If you have HCV genotype 1 or 4 and are co-infected with HIV you should know that the recommended standard of care for HCV is Sovaldi™ (Sofosbuvir), combined with pegylated interferon and Ribavirin. Alternative treatment options exist including options for patients that cannot tolerate Pegylated interferon. Please discuss these other treatment options with your doctor.

WITHDRAWAL FROM STUDY AND REFUSAL TO PARTICIPATE

Taking part in this clinical research study is voluntary and you can refuse to take part or stop at any time without stating a reason. Your withdrawal will not affect your access to other medical care to which you would otherwise be entitled. If you decide to leave the research study, you are strongly urged to:

- Tell your Study Doctor.
- Return to the Study Doctor for one more visit. You will have an exam and plan for your HCV/HIV care.
- Return all unused study drug and study supplies to the Study Doctor.

Your Study Doctor may withdraw you from the study if it is considered important for your medical safety. If it is discovered that you did not give an accurate medical history or did not follow the instructions for the study given by your Study Doctor, you may be taken off the study at any time. If you are taken off the study, you will no longer receive the study drug. Other reasons your Study Doctor may withdraw you from the study include: you need additional medication, you become pregnant or begin breastfeeding, you do not consent to continue in the study after being told of changes in the research that may affect you, or for any other reason. If you are taken off the study, you will no longer receive the study drug.

Your Study Doctor will supervise any discontinuation of the study drug with your health as the first priority. Your taking part in this study may be terminated at any time by a) your Study Doctor, b) Gilead Sciences, Inc., c) FDA or other government agency, d) the Institutional Ethics Committee or Institutional Review Board (a review group that gives approval to your Study Doctor to conduct this study), and other appropriate regulatory agencies.

COST OF TREATMENT

The study drug SOF/LDV FDC used in this study will be given to you free of charge. All clinic, professional, diagnostic, and laboratory fees for tests and procedures (including the liver biopsy, if needed) 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 including all other prescription medications.

PAYMENT FOR PARTICIPATION

You will be paid $50.00 for each completed study visit. Thus if you attend all 12 required visits for the study, the maximum payment you can receive is $600. If you need to come in for an unscheduled visit that is requested by the study staff, you also will be paid $25 for that visit.

In order to be compensated for your participation in this study, you must provide your Social security Number. Additionally, please note that the University of Pennsylvania is required to report to the IRS any cumulative payments for participation in research studies that exceed a total of $600 in a calendar year.

INJURY DURING THE STUDY

All side effects, injuries or illnesses that occur while you are taking part in this research study

If you have a medical emergency during your participation on this study, you should go to the nearest emergency room. You should contact the Principal Investigator or Emergency contact listed on page one of this form. You may also contact your own doctor, or seek treatment outside of the University of Pennsylvania. Be sure to tell the doctor or his/her staff that you are in a research study being conducted at the University of Pennsylvania. Ask them to call the telephone numbers on the first page of this consent form for further instructions or information about your care.

The University of Pennsylvania will offer you the care needed to treat side effects and/or injuries that occur while you are taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them. There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury.

Research-related injuries or illnesses that occur while you are taking part in this research study
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 shown below in the event you experience any study-related illness or injury.

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. Positive tests for both HIV and HCV infection, as well as any CD4 or HIV viral loads done as part of ongoing study evaluations, by law, are to be reported 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.

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 HCV (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, date of birth, email addresses, MRN number
- Social Security Number (if you receive more than $600 for participating in studies at PENN, we will need your SSN for the W-9)
- 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.

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.

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.

Commercial Issues
The University of Pennsylvania receives compensation from the Sponsor, Gilead Sciences, Inc., for having subjects take part in this study.

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.

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.

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).

STORAGE AND USE OF BIOLOGICAL SAMPLES

A portion of your blood drawn and urine collected at study visits will be frozen and stored. Your stored samples and the information collected about you during the study may be used by the Study Sponsor or its research partners for purposes of this study.

Option: 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 has worked against Hepatitis C and HIV. From these samples, it might also be possible to learn more about what causes Hepatitis C and HIV, how to prevent Hepatitis C and HIV, or how to better treat Hepatitis C and 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, an additional 12 mL (approximately 1 Tablespoon) of blood will be drawn at Baseline/Day 1 prior to the first dose of study drug and again at the Early Termination or Week 12 visit. 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, and sign your name 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

_____ _____ _____

Subject Printed Name Signature Date

GS-US-337-0115: Sofosbuvir/Ledipasvir Fixed-Dose Combination for 12 Weeks in Subjects with Chronic Genotype 1 or 4 HCV and HIV-1 Co-infection

AGREEMENT TO BE IN THE STUDY

By signing this informed consent form, I acknowledge that:

(1) I have carefully read and understand the information presented in this consent document.
(2) The purpose and procedures related to this research study have been fully explained to me and I have had the opportunity to ask questions and all of my questions were answered to my satisfaction.
(3) I have been informed of the parts of the program that are investigational and of the possible discomforts, symptoms, adverse events and risks that I might reasonably expect, and the possible complications, if any, that I might reasonably experience from both known and unknown causes as a result of my participation.
(4) I understand that I am free to withdraw this authorization and to discontinue my participation in this program any time. The consequences and risks, if any, of withdrawing from the program while it is ongoing have been explained to me.
(5) I understand that such withdrawal will not affect my ability to receive medical care to which I might otherwise be entitled.

Subject

Subject Printed Name	Signature	Date

Person Obtaining Consent

Printed Name & Title	Signature	Date

Witness (if applicable)

Witness Printed Name	Signature	Date