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

Retreatment Substudy (24 Week Treatment)

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 have already agreed to volunteer for a clinical research study, GS-US-337-0115, involving a new investigational fixed-dose combination (FDC) tablet, called Sofosbuvir/Ledipasvir FDC, for the treatment of chronic Hepatitis C virus (HCV) infection in subjects who are co-infected with Human Immunodeficiency Virus (HIV).

The purpose of this consent form is to give you information about an optional Retreatment Substudy that will be conducted with subjects already enrolled in the GS-US-337-0115 main study who have confirmed detectable HCV during the Post- Treatment phase of the study. This consent form is an addition to the Subject Information and Informed Consent Form for the main study that you have already signed.

This optional clinical research Retreatment Substudy involves a fixed-dose combination (FDC) tablet which combines two investigational drugs called Sofosbuvir (SOF) and Ledipasvir (LDV) into one tablet for the treatment of the Hepatitis C virus (HCV) in subjects who are co-infected with Human Immunodeficiency Virus (HIV). 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). This study also involves the use of Ribavirin (RBV), a drug that is currently approved by the US FDA and is used together with Pegylated Interferon for the treatment of HCV. You will not receive Interferon while on this study.

This Subject Information and Informed Consent Form tells you about the Retreatment Substudy. 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.

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.

GS-US-337-0115: RETREATMENT STUDY Sofosbuvir/Ledipasvir Fixed-Dose Combination + RBV for 24 Weeks in Subjects who still have detectable HCV

PURPOSE OF THE STUDY

The purpose of this Retreatment Substudy is to see if Sofosbuvir/Ledipasvir fixed-dose combination (SOF/LDV FDC) given in combination with Ribavirin (RBV) for 24 weeks is safe and able to clear the Hepatitis C virus (HCV) from HCV/HIV co-infected subjects who had previously participated in the main study and their HCV has still not been cleared from their body. The current standard of care for persons with HCV genotype 1 or 4 is Sovaldi™ (Sofosbuvir), pegylated interferon and RBV.

DESIGN OF THE STUDY

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. The Study Doctor will determine if you are eligible to take part and whether you are eligible to take RBV. Treatment with RBV is not allowed in women who are pregnant or in males whose partner is pregnant, people with low hemoglobin or have kidney problems. The decision to use RBV would be the same if you were not in this study.

This is an "open-label" study, which means both you and your Study Doctor will know what study drug you are taking. If you agree to take part in this study and meet all of the requirements you will receive SOF/LDV FDC and RBV (if possible) daily for 24 weeks.

The study drugs SOF/LDV FDC and RBV will be supplied by Gilead Sciences, Inc., which is the Sponsor of this study. The Sofosbuvir 400mg/Ledipasvir 90mg FDC tablet should be taken by mouth once a day with or without food. The Ribavirin must be taken by mouth twice a day with food at a total daily dose ranging from 1000 to 1200 mg (5 or 6 tablets a day), depending on how much you weigh. Your Study Doctor will let you know how much RBV you should take.

You should never crush or split any of your study tablets. Your Study Doctor may advise you to take fewer tablets, depending on your lab results or adverse events that you may experience.

All the study drugs 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 48 weeks. This study is made up of the following parts:

- Study Treatment: 24 weeks of study drug treatment; includes 8 visits lasting 1 to 2 hours each
- Follow-Up: 24 weeks of follow-up after your last dose of study drug; includes 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:

Study Treatment

Day 1 (1st day of taking study drug)

At this visit, you will discuss and have time to review this consent form in detail. 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.

Your Study Doctor will do some tests or procedures (described below) to see if you meet the requirements for being in the Retreatment Substudy. The Day 1 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
- Blood samples will be taken by a needle stick into a vein in your arm. During the entire Retreatment Substudy, approximately 560 mL (approximately 38 Tablespoons) of blood will be taken. Approximately 55 mL (4 Tablespoons) of Your blood will be collected at your Day 1 visit 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)
    - Coagulation tests to measure the ability of your blood to clot
- 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
- If you still meet all the study requirements, you will be asked to take the first dose of study drug(s) in the Study Doctor's office. You will be given instructions on how to take the study drug(s) at home.

Study Treatment Phase

The study treatment will last for 24 weeks. Study treatment visits are scheduled at the end of weeks 2, 4, 8, 12, 16, 20 and 24. The study staff will instruct you when to return for your next visit per the study plan. Depending on which study visit you are on, you will have between 24 and 46 mL (1.5 to 3 Tablespoons) of blood drawn.

The following will occur at the visits 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(s), 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.
- At every 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 every 4 weeks.
- 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 weeks 4, 8, 12, 16, 20, and 24):
    - 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, 12, 16, 20, and 24
  - Coagulation test, at week 24, to measure the ability of your blood to clot
- 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 4, 8, 16 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 every 4 weeks, if you are a woman who could become pregnant
- You will be counselled on pregnancy prevention at week 24

You may be asked by your Study Doctor to stop taking the study drug(s) 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 enough 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(s), 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 will be collected for [Approximately 46 mL (3 Tablespoons)]:
  - 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)
  - Coagulation tests to measure the ability of your blood to clot
- 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

Follow-Up:

You will return to the clinic for follow-up visits starting 4 weeks after your last does of study drug(s), 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(s). Each visit will last about 1 to 2 hours. Depending on which study visit you are on, you will have between 24 and 46 mL (1.5 to 3 Tablespoons) of blood drawn

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, including blood and protein, 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, if you are a woman who could become pregnant
- Women who took RBV will be provided with urine pregnancy test kits for use between scheduled follow-up visits. You should take a pregnancy test every 4 weeks until 6 months after your last dose of ribavirin. If you have a positive test result you must contact the study clinic immediately and get a blood test to confirm your pregnancy test results.

After all the Post-Treatment visits have been completed, you are done with this Retreatment Substudy.

If the Hepatitis C virus is clear from your blood by the end of the Retreatment Substudy, 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 Retreatment Substudy, 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.

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.

Drugs that affect Hepatitis C virus may not completely remove the virus from your body. If that happens, your Hepatitis C virus may develop drug resistance. Drug resistance may affect your ability to respond to future drugs if they are similar to SOF or LDV.

Sofosbuvir (SOF) Common Adverse Events

The safety profile of SOF in patients is based on the combined safety data from 4 studies where it was given for 12-16 weeks. In these studies, SOF was given at 400 mg once a day in combination with ribavirin (RBV) to 664 patients and in combination with RBV and pegylated interferon alfa 2a (PEG) to 327 patients.

In patients taking SOF with RBV for 12-16 weeks, the most commonly reported side effects of these drugs were (≥10%) were fatigue (41%), trouble sleeping (18%), and irritability (10%).

In patients taking SOF with RBV and PEG for 12 weeks, the most commonly reported adverse drug reactions (≥10%) were:

- fatigue (59%)
- headache (36%)
- nausea (34%)
- trouble sleeping (25%)
- low red blood cell count (21%)
- decreased appetite (18%)
- fever (18%)
- rash (18%)
- chills (17%)
- decreases in the blood cells that fight infection (17%)
- itchiness (17%)
- flu-like illness (16%)
- joint pain (14%)
- muscle pain (14%)
- dizziness (13%)
- irritability (13%)
- diarrhea (12%)
- shortness of breath (12%)
- vomiting (12%)
- cough (10%)
- pain (10%)

Most of these side effects were considered to be mild. These side effects overall were similar to those seen in subjects who took PEG and RBV without SOF. About one in forty subjects taking SOF, RBV, and PEG had to stop their study medications early because of side effects. About one in sixty-five subjects taking SOF and RBV had to stop their study medications early because of side effects. Most of these side effects were believed to have been caused by PEG or RBV.

Ledipasvir (LDV) Common Adverse Events
Ledipasvir has been given alone or with other investigational drugs to over 1000 HCV-infected patients.

The most common side effect reported (>10%) in about 465 subjects taking LDV with other investigational drugs and RBV for at least 12 weeks were:

- Fatigue (Tiredness)
- Headache
- Nausea
- Rash
- Insomnia (Trouble sleeping)
- Pruritus (Itchy)

In about 620 chronic Hepatitis C infected subjects, who took LDV with other investigational drugs, RBV and PEG for up to 24 weeks the most common side effects (>15%) reported, including those listed above, were:

- Irritability
- Myalgia (Muscle pain)
- Flu-like symptoms (see RBV below)
- Decreased appetite
- Fever
- Cough
- Diarrhea
- Anemia (a decrease in the number of red blood cells in your body that carry oxygen). This may cause tiredness and lack of energy.

Most of these side effects were considered to be mild. These side effects overall were similar to those seen in subjects who took PEG and RBV without LDV. Most of these side effects were believed to have been caused by PEG or RBV. You will not receive PEG in this study and you might not receive RBV either.

Rare, but serious:

- Three patients who were taking PEG, RBV, plus two direct-acting antiviral agents (four drugs at the same time), developed pancytopenia (significant decrease in white blood cell count, red blood cell count, and platelet count in the blood). One of these 3 patients was taking LDV (one of the drugs used in this study) plus another direct-acting antiviral agent plus RBV and PEG. The other 2 patients who developed pancytopenia were receiving 2 direct-acting antiviral agents not being used in this study, plus RBV and PEG. The white blood cell count, red blood cell count, and platelet count eventually returned to normal in these patients, but this took several weeks to several months. During this time, the patients needed to receive multiple, repeated blood transfusions until their bone marrow (the body's source of white cells, red cells, and platelets) healed. Because of the risk for possible infection, bleeding, and other complications related to pancytopenia, these subjects needed to be hospitalized. In this study, you will not be receiving PEG, RBV, plus two direct-acting antivirals. You may, however, receive RBV plus two direct-acting antivirals.

- One death, due to bleeding in the head, was reported within 30 days following treatment with PEG, RBV, GS-9451 (an investigational drug), and LDV. The patient, a 59-year-old male, had high blood pressure before starting the study drugs. He went to the emergency room with a sudden onset headache and paralysis of his left arm. The computed tomography (CT) scan at the hospital showed bleeding in his brain. Pegylated interferon has been associated with similar events and this event was considered related to all the study drugs.

Combination of Sofosbuvir and Ledipasvir (SOF/LDV) Common Adverse Events

Sofosbuvir with LDV have been given as two separate tablets and as one fixed-dose combination (FDC) tablet to over 2000 subjects. In the first part of one study, 200 patients who were being treated with the FDC were evaluated 12 weeks after starting therapy. In this group, the most common adverse events that occurred in more than 15% of subjects were headache (29%), fatigue (22%), and nausea (19%).

Rare, but serious:

- One healthy volunteer developed significantly elevated liver tests (ALT) consistent with liver damage while taking SOF/LDV with abacavir/lamivudine (medications used to treat HIV). The patient's liver tests were normal after taking 10 days of SOF/LDV and then were elevated after taking another 5 days of SOF/LDV with abacavir/lamivudine. All study drugs were stopped and his liver tests improved a little but stayed elevated. Two weeks later, the patient had abdominal (belly) pain. An ultrasound showed he had gallstones and mild inflammation of the gallbladder. His gallbladder was removed. His liver tests completely returned to normal only after his gallbladder was removed. We do not know why he had elevated liver tests. The investigator thought that the elevated liver tests were related to SOF/LDV and abacavir/lamivuidine. However, the volunteer's gallbladder disease may have played a role.

- One HCV-infected person developed superior mesenteric vein thrombosis (a clot in the blood vessel that drains blood from the small intestine) during treatment with SOF and LDV. The patient was a 52 year-old man with cirrhosis of the liver. About two weeks after starting treatment, he developed abdominal pain and then nausea and vomiting. The CT scan at the hospital showed a clot partially blocking a vessel draining blood from the small intestine. He was treated with pain medication and blood thinners. The event was considered to be related to the study drugs.

Ribavirin Common Adverse Events

Ribavirin is usually taken with PEG (a once per week shot, which you will not receive during this study).

The most common side effects when taking RBV combined with PEG are flu-like symptoms consisting of:

- Body aches and pains
- Fever
- Chills
- Headache
- Overall feeling of sickness
- Rash

Other common side effects are: anxiety, mood changes, depression and irritability.
The most serious side effect seen with RBV is anemia (a decrease in the number of red blood cells in your body that carry oxygen). This may cause tiredness and lack of energy. 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 these side effects may suggest a serious or fatal health problem.

Ribavirin can cause severe damage and even death of an unborn child or fetus. **Extreme care should be taken to prevent pregnancy while you are taking RBV and afterwards.**

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 to have your chest shaved for this procedure.

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.

The use of RBV during pregnancy is known to increase the risk of birth defects and miscarriage. These effects are seen in animals with very low doses of RBV (one-twentieth of the recommended human dose)

and low levels of RBV can remain in the body for as long as 6 months after the last dose is administered. Ribavirin is also excreted in semen, so if your sexual partner becomes pregnant, it may harm the unborn baby.

For subjects taking only Sofosbuvir and Ledipasvir, 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). **For female subjects who are taking ribavirin, extreme care must be taken to avoid pregnancy during this study and for up to 6 months after the last dose of ribavirin. For male subjects who are taking ribavirin, extreme care must be taken to avoid pregnancy in female partners during this study and for up to 7 months after the last dose of ribavirin.**

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 Day 1 visit) and for a minimum of 6 months after the last dose of ribavirin or 30 days after last dose of study drug if not taking ribavirin, 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. 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. Your Study Doctor will discuss with you other methods of birth control that can be used in combination with a condom.

Women who can get pregnant must have a negative pregnancy test at screening and at the 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 phase of the study. Female subjects taking ribavirin who can get pregnant will receive urine pregnancy test kits at the post treatment week 4 visit to continue pregnancy testing every 4 weeks at home until 6 months after last dose of ribavirin. You will need to report the results of these tests to the study clinic staff during follow-up calls every 4 weeks.

You must tell your Study Doctor immediately if you become pregnant while in this study and for a minimum of 6 months after the last dose of ribavirin or 30 days after the last dose of study drug if not taking ribavirin, 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 7 months after the last dose of ribavirin or 90 days after the last dose of study drug if not taking ribavirin, or longer as directed by your Study Doctor. You must use a condom while your female partner uses 1 other method of birth control. 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 7 months after the last dose of ribavirin or 90 days after the last dose of study drug if not taking ribavirin, 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 7 months after the last dose of ribavirin or 90 days after the last dose of study drug if not taking ribavirin, 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 7 months after the last dose of ribavirin or 90 days after the last dose of study drug if not taking ribavirin.**

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 drugs SOF/LDV FDC taken alone or with RBV 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 when taken alone or with RBV 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 you should know that:

- The current standard of care is Sovaldi™ (Sofosbuvir), pegylated interferon and RBV
- It is not known if the investigational drug combination in this study is more or less safe or if it works as well as the current standard of care

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 drugs SOF/LDV FDC and RBV 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 including all other prescription medications

PAYMENT FOR PARTICIPATION

You will be paid $50.00 for each completed study visit. Thus if you attend all 11 required visits for the study, the maximum payment you can receive is $550. 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.

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 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.

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