UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

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 AN OPTIONAL PHARMACOKINETIC (PK) SUBSTUDY AND RESEARCH SUBJECT HIPAA AUTHORIZATION

Your contacts for this study are:

Site address: 502 Johnson Pavilion, Philadelphia, PA 19104

Principal Investigator: Pablo Tebas, MD (215) 349-8092
Project Manager: Joseph Quinn, RN, BSN (215) 349-8092
Study Nurses: Yan Jiang, RN, BSN (215) 349-8092

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

INTRODUCTION

You have already agreed to volunteer for a research study, GS-US-337-0115, involving a new investigational fixed-dose combination (FDC) pill, 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 pharmacokinetic (defined later) substudy that will be conducted with a small number of subjects enrolled in the GS-US-337-0115 main study. This consent form is an addition to the Subject Information and Informed Consent Form for the main study that you have already signed.

The optional pharmacokinetic substudy is explained below.

Your Study Doctor or Study Nurse will go over this consent form with you and answer any questions you may have regarding this substudy. Before you agree to take part, 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 optional pharmacokinetic sampling, how your participation may help you, any potential risks to you, and what is expected of you during the substudy.

This consent form describes the optional pharmacokinetic substudy and the additional procedures that will be performed if you agree to participate. If you agree to take part in the substudy, 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 the substudy. Even if you agree to participate, you are free to change your mind and stop at any time without penalty or loss of benefits which you would otherwise have. You can still continue to participate in the main study even if you do not agree to participate in the substudy. You must have reviewed and signed the main study consent before signing this consent. This consent form is not meant to replace the main study consent, and the contents of the main study consent apply to these substudy.

PURPOSE OF THE Pharmacokinetic (PK) SUB-STUDY

This Pharmacokinetic (PK) Substudy will be conducted in subjects already enrolled in the GS-US-337-0115 main study. All enrolled subjects may be eligible to participate.

Blood will be drawn to determine the concentration (amount) of the study drug and HIV antiretroviral (ARV) medication in your body. This type of testing is called pharmacokinetics and measures the amount of the drug in your blood and tells the researchers how much time it takes for the drug to be absorbed
into your body, how long it stays in your body after it has been absorbed and how different drugs interact with each other in the body.

This research is important to doctors like yours because it can help your doctors understand why some people (like you) might benefit differently from some medicines while others do not. Sometimes this research can also help explain why some patients are more likely to have a bad reaction to medicines.

**SUB-STUDY PROCEDURES**

The PK substudy will occur once in the study and will take place as an add-on to the main Study Treatment Week 2, 4, 6 OR 8 visit (after you have started taking the study drug). Blood samples will be collected over a 24 hour period at the following time points: before you take the Sofosbuvir/Ledipasvir FDC (SOF/LDV FDC) dose and/or your HIV ARV medication, and then again at 30 minutes and 1, 2, 4, 8, 12 and 24 hours after taking SOF/LDV FDC and/or your HIV ARV medication (a total of 8 times). A total of approximately 64 mL (about 4.5 tablespoons) of blood will be drawn.

(Please note that these procedures are in addition to the regularly scheduled procedures that will take place for the main study).

If you participate in the PK substudy, you will be asked to take the SOF/LDV FDC pill and your HIV ARV medication at the same time of the day (morning or evening depending on when you typically take your HIV ARV medication) every day for at least the 10 days before your scheduled PK substudy visit.

You will be asked to complete a dosing diary every time you take your medications. You will have to complete the diary with the date, time and how much medication you have taken each day.

You will need to “fast” before your PK substudy visit. “Fasting” means no food or liquids (except for water) for at least 8 hours before your PK substudy visit. You will also be asked to bring your study drug and your HIV ARV medication to the clinic for this visit.

On the day of your PK substudy visit, **DO NOT** take your applicable dose of SOF/LDV FDC and/or HIV ARV medication before going to the clinic. Once at the clinic, you will take your dose of SOF/LDV FDC and/or HIV ARV medication and be allowed to eat when told by the Study Doctor or study staff. You will not be allowed to eat any food again until after the 4-hour blood draw.

You may be required to stay overnight at the clinic for the PK substudy. After the 12 hour blood draw of the PK substudy visit, you may leave the clinic when the Study Doctor or study staff believes it is safe for you to do so and return for the 24 hour blood sample collection or you may be asked by the Study Doctor or study staff to stay at the clinic until the 24 hour blood sample is collected.

**What will happen to your blood sample?**

Your sample(s) will be labeled with a code. Your identity will be protected and your name will not be attached to the sample. The sample will be prepared and stored in a freezer for future pharmacokinetic testing for up to 10 years. After 10 years, the sample will be destroyed.

**RISKS**

**BLOOD DRAWS**

Possible side effects from blood drawing include dizziness, redness and swelling of the vein, pain, bruising or bleeding from the site of the needle puncture site. Rarely, a clot or infection could occur that would require treatment. Some people feel faint or sick when blood is taken.
POSSIBLE BENEFITS
There is no direct benefit to you from participating in the substudy. Your participation in the substudy may benefit the community, scientists, and doctors who work with Hepatitis C by providing increased knowledge and information about the treatment of your disease and SOF/LDV FDC.

WITHDRAWAL FROM STUDY AND REFUSAL TO PARTICIPATE
Like your participation in the main research study, the substudy is completely voluntary. You may participate in the main research study EVEN IF YOU ARE NOT PART OF THE SUBSTUDY. Your decision will not affect future treatment you may receive or your rights as a research subject.

The results of your tests from the substudy will NOT be available to you or your Study Doctor and you will not be notified of any findings related to your sample since the testing is completely for research.

If you consent to this substudy and decide at a later date that you would like to withdraw your consent, you will need to do so in writing to your Study Doctor.

Withdrawing consent will result in destruction of your substudy sample(s). 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 us 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 sample(s) you provided for PK research testing will continue to be available for testing unless you also withdraw your consent for the substudy as stated above.

PAYMENT FOR PARTICIPATION
You will be paid $100.00 for the first day of the PK substudy. If you stay overnight, you will get $50 for the second day or if you return on the second day, you will also get $50. Total compensation for the PK study will be $150. This will be in addition to your regular visit.

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. 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
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
- 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.

AGREEMENT TO BE IN THE STUDY

By signing this informed consent form, I acknowledge that:

1. I agree to have my substudy sample(s) stored up to 10 years.
2. I understand that I will not receive results from the substudy nor will the Study Doctor in charge of the main research study.
3. I understand that the Study Doctor and Gilead Sciences, Inc., the Sponsor of these research studies, do not have any plans to compensate me in the event that a commercial product is developed by this substudy research.

If you answered NO to any of the questions listed above you should not sign this form. Once you have had all your questions answered and you are comfortable participating in the substudy, please sign below.

Subject

Subject Printed Name __________________________ Signature __________ Date __________

Person Obtaining Consent

Printed Name & Title __________________________ Signature __________ Date __________

Witness (if applicable)

Witness Printed Name __________________________ Signature __________ Date __________

Page 6 of 6