

# IMPORTANT

**PLEASE READ YOUR ENTIRE APPROVAL PACKET THOROUGHLY,  
PAYING SPECIAL ATTENTION TO THE APPROVAL LETTER.  
THE LETTER CONTAINS INTEGREVIEW'S REPORTING  
REQUIREMENTS WITH WHICH YOU ARE OBLIGATED TO COMPLY.**

**IN ADDITION, IT IS YOUR RESPONSIBILITY TO ENSURE THAT  
PERIODIC CHECKS ARE DONE IN IRBMANAGER TO CONFIRM YOU  
ARE UTILIZING THE MOST CURRENT INFORMED CONSENT.**

To access request forms and/or obtain your IRB documents, you will always start from your Home page:

- Click on the specific protocol number you wish to submit for; which can be found under 'My Protocols'.
- Once you click on the protocol, it will re-direct you to the Study Summary Page (SSP).

## **Obtaining documents from IRBManager:**

To obtain your IRB action letter, including new/updated informed consents when applicable, once on the SSP you can:

- Scroll down to the 'Events' tab
- You can click on the Event itself or on the number listed in the column labeled "Att" (i.e. attachments)
- Approval documents will be listed under the sub-heading "IntegReview Approval Documents"

## **Submitting on IRBManager:**

All request forms (other than New Study Submission Forms) are protocol driven. You can obtain by:

- Clicking on 'Start xForm' - Under 'Actions' (left side of screen)
- Select the appropriate xForm (listed alphabetically)



## **IRB Statement of Compliance**

IntegReview IRB, an independent IRB located in Austin, Texas, was established in 1999 and offers five weekly meetings for review of U.S. and Latin American research, an “as needed” meeting for review of Canadian research, quality review by experienced individuals, competitive fees, and quality assurance/control. Designed to accelerate the IRB process without compromising accuracy or the protection of human subjects, IntegReview IRB delivers study documents to the investigator within two business days of board review.

IntegReview IRB is committed to meeting rigorous standards for quality and maintaining sound policies and procedures involved in the protection of human research participants. IntegReview IRB was initially awarded full accreditation of its human research protection program (HRPP) by the Accreditation of Human Research Protection Programs, Inc.,<sup>®</sup> (AAHRPP) in June 2007. AAHRPP accreditation will expire in September of 2020.

Written standard operating procedures govern IntegReview IRB for initial, continuing, full board, expedited and exempt review of clinical research studies. IntegReview IRB complies with the regulations as defined in the United States Food and Drug Administration (FDA), Code of Federal Regulations, Title 21, Parts 50, 54, 56, 312 and 812, International Conference on Harmonisation (ICH) Guidelines for Good Clinical Practices, E6, the Department of Health and Human Services (DHHS) regulations as identified in the Code of Federal Regulations, Title 45, Part 46, other regulations as applicable, Health Canada Regulations/Guidelines, as well as local and state laws.

A handwritten signature in black ink that reads "Lynn A. Meyer". The signature is written in a cursive style.

Lynn A. Meyer, CCRP  
President



March 17, 2016

Principal Investigator: Fred Poordad, M.D.

Sponsor: American Research Corporation at Texas Liver Institute

Protocol Number: TLI\_IIS\_01\_2015

Study Title: "A study to investigate HCV response rates in real world patients traditionally excluded from clinical trials: The HEARTLAND Study"

Dear Dr. Poordad:

A convened IRB meeting of IntegReview was held on the above-referenced date. The following full board action was taken on initial review of the above-referenced study:

Approved:

Principal Investigator

Investigative site(s) as submitted with initial submission documents

Protocol dated 12 February 2016

Informed Consent, English language, dated March 17, 2016, (refer to IntegReview modifications as reflected on the following document containing revision marks)

Recruiting/miscellaneous materials:

One questionnaire

IntegReview does not review stand alone HIPAA documents. Federal regulations do not require IRBs to review and approve stand-alone HIPAA authorizations. Following is a website presenting the IRBs role under the Privacy Rule from the National Institutes of Health: <http://privacyruleandresearch.nih.gov/irbandprivacyrule.asp>. Please refer to paragraph 12, which identifies IRB obligations regarding these stand-alone documents.

The Board reviewed the package insert and drug information, for the study drug(s), as appropriate.

#### IMPORTANT

- **The following changes in approved research may not be implemented until you have received approval from IntegReview except where necessary to eliminate apparent immediate hazards to the human subjects:**
  - **Protocol Amendments**
  - **Change in the Principal Investigator and/or Sub-investigators (only if the Sub-investigators will be performing study-related procedures that the PI is not qualified through expertise to perform)**
  - **Change in the address at the study site or the addition of a study site(s)**
- **Only Informed Consent documents containing IntegReview's approval stamp may be utilized:**
  - **There must be procedures in place to guarantee that consent has been voluntarily obtained and properly documented.**

3815 S. Capital of Texas Hwy, Suite 320, Austin, TX 78704  
Tel. 512.326.3001 Local Fax. 512.697.0085 <http://www.integreview.com>

IRB Registration Numbers: IRB00008463, IRB00003657, IRB00004920, IRB00001035, IRB00006075



- **For participants that do not speak English, the informed consent document must be in a language understandable to them.**
- **Only IntegReview staff may initiate modifications to Informed Consent documents. The Informed Consent document for your site will be maintained in our computer files, and IntegReview will make all revisions following board approval.**
- **Only recruiting materials containing IntegReview's approval stamp may be utilized. All audio/video recording(s) must be submitted for IRB approval prior to broadcast.**
- **Revision requests should be submitted on IntegReview's forms, which are available in IRBManager.**
- **Visit our website at [www.integreview.com](http://www.integreview.com) for information on research regulations, reporting requirements, Investigator and research personnel training, etc.**

IntegReview approval for this study expires **March 16, 2017**.

In order to obtain extended IRB approval, IntegReview must receive your form for continuing review two weeks prior to the IRB expiration date. Appropriate forms will be forwarded to you approximately four weeks prior to the approval expiration date. Should the study end before you receive notification, submit a Closure Notification form.

## **REPORTING REQUIREMENTS**

To ensure compliance with the applicable federal regulations as well as International Conference on Harmonisation (ICH), E6: Good Clinical Practice: Consolidated Guideline, and/or IntegReview's requirements, notification of the following are required for review/approval:

- **Report immediately:**
  - Changes in research that were initiated without IRB review and approval to eliminate apparent immediate hazards to the human subjects to ensure the continued safety and welfare of subjects
  - Modifications to previously approved documents
  - Receipt of investigator/site 483, Determination letter or Warning letter
  - If your license is suspended, revoked, placed on probation or restricted in any state or country
  - Safety information that may help to provide additional protections for subject's safety and well-being, throughout the course of the study and after study completion.
  - Communication of results from a research study to subjects when those results directly affect their safety or medical care
  - Reports of pregnancy
- **Report within 10 calendar days of discovery:**
  - Revisions to the Investigator's Brochure, as applicable
  - Revisions to the report of prior investigations, as applicable
  - Non-compliance – Failure by an investigator and/or sponsor to follow IntegReview's requirements, applicable regulations or to protect human research subjects, including but not limited to the principles of the Belmont Report
  - Serious non-compliance issues - non-compliance as defined as above and as determined to be serious in a way that adversely affects the rights and welfare of human subjects following the investigation and review by the IRB
  - Continuing non-compliance issues – A pattern of repeated non-compliance or serious non-compliance as determined by the IRB

- Significant deviations – Significant deviations are those that deviate from the approved protocol, informed consent process and affect or potentially affect the safety of subjects. IntegReview does not consider protocol deviations to be different from protocol violations.
- Unanticipated adverse device effects, as applicable
- Unanticipated problems should be reported regardless of whether they occur during the study, after the study completion, or after participant withdrawal or completion. Unanticipated problems involving risks to human subjects or others that are (1) unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied; (2) related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures in the research); and (3) suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized. Examples of problems or events that may meet the definition of unanticipated problems involving risk to subjects or others may include, but are not limited to the following:
  - Imminent threat of a reportable event that has not yet occurred
  - Information indicating a change to the risk/benefit ratio of the research
  - Death
  - Breach of confidentiality, including lost or stolen study documents/data
- **Report within 30 days of acquisition or discovery**
  - New or additional conflicts of interests
- **Submit prior to publication/distribution:**
  - Any modification(s) to the previously approved Informed Consent document
  - New and/or modifications to previously approved recruiting/miscellaneous materials to be seen or heard by subjects
- **Submit two weeks prior to IntegReview approval expiration date:**
  - Continuing review documents
- **Submit upon completion of the study:**
  - Notification of study closure

At its discretion, IntegReview IRB reserves the right to visit the study site.

IntegReview IRB is organized and operates in accordance with the applicable federal regulations, and ICH Guidelines for Good Clinical Practices, E6. In addition, Standard Operating Procedures have been created to ensure compliance with these regulations and guidelines.

If you have any questions regarding these procedures or if you wish to appeal the decision of the Board, you may address your comments to the IntegReview Chair. Your comments will be reviewed and discussed at the next convened meeting.

**Failure to comply with the Code of Federal Regulations or the requirements or determinations of IntegReview IRB can result in suspension or termination of IntegReview approval.**

Sincerely,

*Rosa S. Sandoval.*

Rosa S. Sandoval, B.S., CCRP  
Senior IRB Coordinator, Co-chair

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

~~-1 February 2016~~

AGREEMENT TO BE IN A RESEARCH STUDY

NAME OF SPONSOR COMPANY: American Research Corporation at the Texas Liver Institute

~~Study Title:~~

NUMBER AND NAME OF STUDY: TLI\_IIS\_01\_2015; "A STUDY TO INVESTIGATE HCV RESPONSE RATES IN REAL WORLD PATIENTS TRADITIONALLY EXCLUDED FROM CLINICAL TRIALS: THE HEARTLAND STUDY"

~~Protocol Number: TLI\_IIS\_01\_2015~~

~~Sponsor: American Research Corporation at the Texas Liver Institute~~

NAME OF PERSON IN CHARGE OF THE RESEARCH STUDY

(INVESTIGATOR/STUDY DOCTOR): Fred Poordad, M.D.

DAYTIME AND AFTER HOURS TELEPHONE: 210-253-3426

~~After Hours: 210-253-3426~~

Before you can make an informed decision to participate in this research study, you should understand the possible risks and benefits of this study. This process is known as informed consent. This consent form contains information about the study and has been reviewed and approved by the IRB, a group of independent experts and lay persons. This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision. If you decide to participate in this study, you will be asked to read and sign this consent form to confirm that you have had the study explained to you, and you have agreed to participate. You will receive a copy of the signed and dated consent form.

Introduction

You are being asked to participate in this research study of FDA approved drugs, VIEKIRA PAK (Paritaprevir/Ritonavir/Ombitasvir tablets; Dasabuvir tablets) and Ribavirin tablets. You are being asked because you have been diagnosed with the chronic genotype 1 hepatitis C virus (HCV) infection and are with or without a diagnosis of compensated cirrhosis (early liver damage in which the body functions normally despite the damaged liver tissue) and either you have not taken medications to treat the HCV infection or you have been previously treated for HCV infection ~~who~~and have failed a regimen including pegIFN/RBV +/- telaprevir, boceprevir, or simeprevir.

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The FDA approved VIEKIRA PAK (ombitasvir, paritaprevir, ritonavir fixed dose combination tablets copackaged with dasabuvir tablets) for use with or without ribavirin for the treatment of patients with genotype 1 chronic hepatitis C virus (HCV) infection.

~~Ombitasvir is a type of drug called an HCV protease inhibitor (which, in this study, will be given with a drug called ritonavir, which boosts the amount of OBV in the blood). Paritaprevir is a type of drug called an HCV NS5A inhibitor.~~ (OBV), ~~ritonavir~~ritonavir (r) and **Paritaprevir (PTV)** will be combined into one pill, known as OBV/PTV/r. ~~Dasabuvir is a type of drug called an HCV polymerase inhibitor. This combination pill will be packaged with Dasabuvir to make the VIEKIRA PAK. In addition to VIEKIRA PAK, you will also receive ribavirin (RBV). Ribavirin is also approved by the FDA for the treatment of chronic HCV in adults. The RBV dose will be given at an investigational dose. "Investigational" means the the dose being given has not been approved by the United States Food and Drug Administration.~~ These drugs are intended to prevent the HCV from multiplying in the human body.

~~In addition to VIEKIRA PAK, you will also receive ribavirin (RBV). Ribavirin is also approved by the FDA for the treatment of chronic HCV in adults. The RBV dose will be given at an investigational dose.~~ Be aware that this form refers to OBV/PTV/r, DSV, and RBV as "study drug."

~~OBV/PTV/r and DSV used with weight based (1000-1200 mg /day) RBV has been approved by the FDA for the treatment of people with genotype 1a (GT1a) chronic hepatitis C virus (HCV) infection without cirrhosis.~~

American Research Corporation is sponsoring this study. Any reference to "American Research Corporation" or "sponsor" in this consent form also means any company that might take over American Research Corporation's interests as sponsor of the study, whether before or after the completion of the study. American Research Corporation is paying the study doctor to perform this study.

Being in this study does not replace your regular medical care.

**You must be honest with the investigator about your health history or you may harm yourself by participating in this study.**

### **Purpose of the Study**

The purpose of this study is to see if the study drugs are safe and able to reduce the amount of HCV in your blood.

### **Study Information**

This study is being conducted as a single center study at American Research Corporation in San Antonio and 2 satellite sites located in Austin and McAllen Texas. This study is designed to enroll approximately 100 ~~subjects~~**men and women ages 18 years and older.**  
~~for scientific, regulatory and ethical reasons.~~

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This is an open-label study. This means that you, your doctor/study staff and the study sponsor, ~~AbbVie~~, will know which drugs you will be receiving.

The study consists of 2 parts: Treatment Period and Post Treatment Period

**Part 1: Treatment Period**

You will be assigned to one of **the** following groups based on the current guidance of the Viekira Pak insert. You will either be in the 12-week treatment arm or the 24-week treatment arm as described below.

12-Week Treatment Arm:

- To include patients with Genotype 1a without cirrhosis, Genotype 1b with cirrhosis.
- VIEKIRA PAK taken by mouth for 12 weeks
- RBV according to package insert:
  - if you weigh less than 165 lbs (75 kg), you will take 1000 mg daily (e.g., two 200 mg capsules in the morning and three 200 mg capsules in the evening) by mouth for 12 weeks
  - if you weigh 165 lbs (75 kg) or more, you will take 1200 mg daily (e.g., three 200 mg capsules twice daily) by mouth for 12 weeks

12-Week Treatment Arm:

- To include patients with Genotype 1b without cirrhosis.
- VIEKIRA PAK taken by mouth for 12 weeks

24-Week Treatment Arm:

- To include patients with Genotype 1a with cirrhosis.
- VIEKIRA PAK taken by mouth for 24 weeks
- RBV:
  - if you weigh less than 165 lbs (75 kg), you will take 1000 mg daily (e.g., two 200 mg capsules in the morning and three 200 mg capsules in the evening) by mouth for 24 weeks
  - if you weigh 165 lbs (75 kg) or more, you will take 1200 mg daily (e.g., three 200 mg capsules twice daily) by mouth for 24 weeks.

**Part 2 Post Treatment Period**

After completing Part 1, you will be monitored for an additional 12 weeks following the last dose of study drugs to see if the hepatitis C virus can still be detected, and if so, whether it has become resistant to any of the study drugs. Resistant means that the drugs are no longer working against the virus.

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**Study Duration**

Your participation in this study will last approximately 24 to 36 weeks (excluding the screening period) dependent upon your treatment assignment. You may need to visit the research center for up to 10 study visits.

**Study Procedures**

If you agree to be in this study, you will undergo some activities, tests and evaluations to determine if you are eligible for this study. Such tests and evaluations listed in the table below are completed during a screening period that takes place before study participation. If you are eligible to participate in this study, you will undergo the other procedures listed in the table below.

**Study Activities**

Activity	Treatment Visits – All Patients								
	Treatment Visits – All Patients					Treatment Visits Patients Requiring 24 Week Treatment			Premature D/C During Treatment Period
	Screening	Day 1/ Baseline	Week 4	Week 8	Week 12 (EOT)	Week 16	Week 20	Week 24 (EOT)	
Informed Consent	X								
Medical History	X	X							
Physical Exam*	X	X			X			X	X
12 Lead ECG*	X	X			X			X	X
Vital Signs	X	X	X	X	X	X	X	X	X
Hematology/Chemistry + Urinalysis/Coagulation Panel Blood and Urine for lab tests	X	X	X	X	X	X	X	X	X
Pregnancy Test [serum blood (sb), urine (u)]	X (sb)	X (u, sb)	X (u)	X (u)	X (u)	X (u)	X (u)	X (u)	X (u)
Drug Screen (urine)	X	X							

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AFP Test	X								
HbsAg/HCV-ab/HIV	X								
HCV Genotype Blood Test	X								
HCV RNA PCR	X	X	X	X	X	X	X	X	X
HCV Resistance Sample (baseline for all; only when detectable HCV RNA during treatment after previously testing negative)		X							
Concomitant Medication Assessment	X	X	X	X	X	X	X	X	X
Randomization		X							
SF36v2 survey (only at baseline and EOT for all patients)		X			X * *			X **	X * *
Adverse Event Side effects Assessment			X	X	X	X	X	X	X
Study Drugs Dispensed		X	X	X	X	X	X		

\*Physical exam and 12 Lead ECG will be performed on all patients at screening, baseline and end of treatment (either Week 12, Week 24 or Early Discontinuation)

\*\*Performed twice for all patients: baseline and EOT (week 12, **or week 24 or early discontinuation**) ~~as the follow up based on patient treatment duration~~

Wk = Week; EOT = End of Treatment; D/C = Discontinuation; PTW = Post-Treatment Week; PT D/C = Post-Treatment Discontinuation

If you are enrolled in 12 week treatment arm you will complete all specified study activities up to 12 weeks. If you are enrolled in 24 week treatment arm you will complete all specified study activities up to 24 weeks.

Note: At every study visit, you will be asked about any change in the medications you are taking, any problems you are having, and any side effects you are experiencing, which may or may not be related to the study or whether you have made any visits to other doctors or hospitals.

**Study Activities (Continued)**

Activity	Post Treatment Week 4	Post Treatment Week 12 or Early PT D/C

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Physical Exam	X	X
Vital signs	X	X
<del>Adverse Event</del> Side effects Assessment	X	X*
HCV RNA	X	X
HCV Resistance Sample (for those with detectable HCV RNA)*		Only in non-SVR patients

\*Only for early post-treatment discontinuations. ~~Adverse event~~Side effect assessment only assessed up to 30 days post-treatment.

**Blood Draws**

The blood samples will be taken by individual needle sticks into one of your arm veins.

You will undergo approximately 10-11 blood draws during the course of this study. The maximum amount of blood taken for the entire study for 12 week treatment period will be approximately 133 mLs. If you are in the 24 week treatment group it is approximately 193 mLs.

**HIV AND HEPATITIS**

If any person is exposed to your blood, you must have your blood tested for the hepatitis viruses and for HIV. HIV is the virus that causes AIDS.

If the HIV test is positive, a follow-up test will be done. If the follow-up test is also positive, you will be told in private and you will also be told about counseling.

It may take weeks or months after being infected with HIV for the test to be positive. The HIV test is not always right.

Positive test results may be required to be reported to the State Department of Health. If you have any questions about what information is required to be reported please ask the investigator or study staff.

Although this testing is supposed to be private, this cannot be guaranteed. For example, it is possible for a court of law to get health or study records without your permission.

**Additional Procedure Information**

- Pregnancy testing: The study doctor or study staff will tell you if the pregnancy test results are positive. The results of the pregnancy testing must be negative in order for you to be in the study.

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**Subject's Responsibilities**

In order for this study to provide good information about how this drug works in subjects with HCV, you will be expected to do the following:

- Follow the instructions of your study doctor.
- Come to all your scheduled study visits and procedures.
- Certain medications you are taking or have taken in the past may keep you from being in this study. You may be required to stop or adjust the dose for certain medications and supplements you are currently taking either prior to starting study drugs or during the study. Please review all of your medications with your study doctor.
- Do not change any of your other medications or start any new medications without checking with your study doctor as certain medications could interact with the study drugs.
- Tell the study staff what procedures/conditions you have had in the past as they may keep you from being in this study.
- Fill out your health-based questionnaires completely and honestly. You will be given one questionnaire at two time points throughout the study to assess what you think of your health and quality of life.
- If you see a doctor outside the research study, tell the doctor you are in an investigational research study as certain medications could interact with the study drugs.
- Tell the study staff about any health problems you are having even if you don't think they are important.
- Tell the study staff if you wish to stop being in the study and come back for the final visit.
- Do not participate in any other studies during your participation in this study.
- At every study visit, you will be asked to provide any changes in the medications you are taking, any problems you are having, and any side effects you are experiencing, which may or may not be related to the study or whether you have made any visits to other doctors or hospitals.

**Study Drug Instructions**

You will receive specific instructions on how to take all of the study drugs in this study. You will have a discussion with your study doctor or study staff about the importance of taking your study drugs at the time and at the dose that your study doctor has instructed. Should you miss taking a dose at a scheduled time, it is important that you tell your study doctor at your next visit. If you decide to stop taking your study drugs, it is very important that you tell your study doctor right away.

- Take and store your study drug as instructed and return the unused study drug and/or empty containers to the study doctor's office at each visit.
- Do not share your study drug with anyone. You are the only person allowed to take the study drug.
- Keep the study drug and study supplies out of the reach of children and persons of limited ability to read or understand.

**NOT TO BE USED FOR SUBJECT ENROLLMENT**

~~If you have questions about your participation in this study or if you think you have had a study related injury or reaction to the study drug, contact the study doctor at the phone numbers listed on page 1 of this Informed Consent Form.~~

~~If you have questions concerning your rights as a research subject, you may contact:~~

~~IntegReview IRB  
3815 S. Capital of Texas Hwy  
Suite 320  
Austin, TX 78704  
Phone: 512-326-3001  
Fax: 512-697-0085  
Email: integreview@integreview.com~~

**Risks and Discomforts**

**If you do not understand what any of these side effects mean, please ask the study doctor or study staff to explain these terms to you.**

**You must tell the investigator or study staff about all side effects that you have. If you are not honest about your side effects, you may harm yourself by staying in this study.**

**~~Data in healthy volunteers~~**

**When you take more than one drug at a time, the side effects can be worse or different than if you take either drug by itself.**

**Until you know how the drugs will affect you, you should use caution by avoiding stairs, not driving a car or working with machinery.**

The most common side effects seen in healthy volunteers taking multiple doses of paritaprevir, ombitasvir, and dasabuvir given together were:

- Headache: 7.3%, about 7 in 100 subjects
- Diarrhea: 3.6%, about 4 in 100 subjects
- Nausea: 2.9%, about 3 in 100 subjects
- Dizziness: 2.9%, about 3 in 100 subjects
- Constipation: 2.5%, about 3 in 100 subjects
- Common cold symptoms: 2.2%, about 2 in 100 subjects

**~~Data in~~ HCV-infected people receiving **similar drug combinations** ~~of AbbVie's HCV drugs~~ in clinical trials **experienced:****

~~Over 5,000 HCV-infected people have received a paritaprevir/r-based interferon-free, combination direct-acting antiviral (DAA) HCV regimen during Phase 2/3 and currently ongoing clinical trials.~~

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~~Side effects which were considered related to the 3 DAA+ ribavirin (RBV) drugs are listed below from most frequent to least frequent. These events occurred at least 5% more often in people receiving 3 DAA + RBV drugs than with people who received a sugar pill (placebo) in the placebo-controlled Phase 3 studies.~~

- ~~• Very common (greater than 1/10):~~
- ~~T~~Tiredness (34.2%, about 34 in 100 people);
- ~~N~~Nausea (22.3%, about 22 in 100 people);
- ~~I~~Itching (15.7%, about 16 in 100 people);
- ~~T~~Trouble sleeping (14.0%, about 14 in 100 people);
- ~~W~~Weakness (13.5%, about 14 in 100 people)
- ~~Common (greater than or equal to 1/100 to less than 1/10):~~ Low blood count (5.3%, about 5 in 100 people)

**~~Data in people receiving combinations of AbbVie's experimental HCV medications~~**

Risk of liver problems and failure:

A small number of participants have experienced severe liver problems while on the Viekira Pak, some of whom died or required liver transplantation. These liver problems included confusion, abdominal fluid accumulation and swelling, bleeding, and changes in blood tests that measure the function of the liver.

It is unknown whether or not these liver problems were directly caused by the Viekira Pak or just as a result of their advanced liver disease. Most participants who died or needed a liver transplant already had advanced disease before starting the Viekira Pak. Blood tests that measure your liver function will be performed during the study, and your study doctor will monitor you for signs of severe liver problems. Let your study doctor know if you have swelling of the stomach area, bleeding, or are feeling confused.

Risk of ALT elevations:

About 1 in 100 participants (1%) receiving Viekira Pak experienced an increase in ALT (a blood test that increases when your liver is inflamed) levels. Increased levels of ALT happened more often in people receiving medicines containing ethinyl estradiol, which many birth control pills contain. These increased ALT levels did not cause symptoms, usually happened during the first 4 weeks of dosing, and got better with continued dosing with the Viekira Pak.

Participants who are taking ethinyl estradiol-containing medicines will be asked to stop taking these medicines before starting dosing with the Viekira Pak. Ethinyl estradiol-containing medicines include pills, patches, or rings that deliver ethinyl estradiol for the purpose of contraception or for other clinical indications, including some hormone replacement therapy. Estrogens used to treat symptoms of menopause like vaginal creams do not typically contain ethinyl estradiol. If you are using an estrogen, it is important for your study doctor to check what type of estrogen it contains.

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If you are taking an ethinyl estradiol containing medication for birth control, your study doctor may switch you to a different method of birth control (for example, a progestin-only containing contraceptive or non-hormonal form of birth control). You may restart your ethinyl estradiol-containing medicine about 2 weeks after your study drug dosing is completed. Your blood levels of ALT will be measured during this study. Let your study doctor know if you have new onset of:

- Fatigue;
- Weakness;
- Lack of appetite;
- Nausea and vomiting;
- Jaundice

**General Information**

The study medications may interfere/interact with some medications, so you must let your doctor know about any medications, herbals or vitamins that you are taking.

**Increased bilirubin levels**

Some people taking the Viekira Pak, especially those who were also taking ribavirin or the HIV medicine atazanavir, had increased levels of bilirubin (a substance measured in your blood that is produced when red blood cells are broken down) which can cause yellowing in the eyes or under the tongue in some people. These bilirubin increases may be temporary and may not be associated with damage to the liver. Increases in bilirubin usually reach their highest level in the first week after starting the Viekira Pak, and get better with continued study drug dosing.

In some cases, increases in bilirubin can get worse. If bilirubin increase occurs with other signs such as swelling of the stomach area, vomiting of blood, or confusion, it may be a sign of a severe liver problem.

**Hemoglobin decreases**

**Ribavirin (RBV)** is known to cause anemia (low hemoglobin levels from having low red blood cell counts). See RBV-related risks. In studies where participants received the Viekira Pak with RBV, hemoglobin levels decreased during dosing and got better after dosing was finished. Low hemoglobin levels were usually treated by decreasing the dose of RBV given. Participants rarely required blood transfusions or other medicines to increase hemoglobin levels.

**General Information**

The study drugs may interfere/interact with some medications. **If you take a calcium channel blocker, you may experience leg swelling after starting the study drugs.** ~~One such interaction is with a type of blood pressure medicine called calcium channel blockers. In studies done in Japanese people, 5% of participants taking calcium channel blockers developed leg swelling, a known side effect of calcium channel blockers, after starting DAA (study drugs).~~



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Some drug interactions may be serious or life threatening. You must let your study doctor know about any medications or vaccines (oral, inhaled, topical, or other), including herbals or vitamins that you are taking.

It is important to remember that the recently approved Viekira Pak is still being studied in humans, so some of the risks of the combinations of ~~AbbVie's HCV~~these drugs are not yet known.

~~In addition, as with any drugs, the Viekira Pak may cause unexpected allergic reactions. Allergic reactions, including lip and tongue swelling, have been observed in people taking the Viekira Pak drugs. See below for more information on allergic reactions.~~

**Information about pregnancy**

Some drugs cause premature (early) birth or birth defects. The risks of ~~AbbVie's Viekira Pak~~the study drugs in pregnancy are not known. However, RBV is known to cause birth defects and can lead to the death of an unborn child - see RBV related risks.

**Ribavirin Study Drug Risks**

Ribavirin has been marketed for HCV infection administered in combination with other HCV drugs (ribavirin is not effective against HCV infection when given by itself). Side effects which may be experienced with RBV include:

- Nausea
- Anorexia
- Vomiting
- Diarrhea
- ~~D~~yspepsia (stomach upset)
- ~~A~~bdominal pain
- ~~I~~nsomnia
- ~~R~~ash
- Hemolytic anemia (decreases in your red blood cells caused by breakdown of your red blood cells). The breakdown of red cells may lead to increased levels of bilirubin, and uric acid (these will show up in lab results). The hemolytic anemia may cause worsening of heart disease which may lead to heart attacks and, sometimes, death.
- Significant birth defects if pregnancy occurs while taking ribavirin or if pregnancy occurs up to 6 months after taking ribavirin.

You should not use ribavirin if you have been diagnosed with blood disorders such as sickle cell anemia or certain other genetic blood disorders which affect your red cells.

If you (or your partner if you are a male study subject) become pregnant or breastfeed during the study while receiving ribavirin, or for 6 months after having received ribavirin, it can have harmful effects on

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fetal development. Because there is a potential risk of fetal death or injury, you should not plan a pregnancy, or breastfeed if you are a female subject or a female partner of a male subject, during the trial and for a minimum of 6 months after the last dose of ribavirin.

~~Note that interferon alpha may enhance ribavirin side effects and the combination of interferon alpha with ribavirin is associated with additional side effects. It is important to note that you will not be taking ribavirin with interferon alpha in this trial.~~

You should get medical help and contact the study doctor or study staff if you have any of these or any other side effects during the study.

It is important to remember that some the risks of ribavirin may not be fully known.

The information provided here only describes some of the side effects reported with RBV. Therefore, you should refer to RBV label for additional risks.

Your study doctor will be monitoring you for side effects from ombitasvir/paritaprevir/ritonavir, dasabuvir and RBV. It is important that you report any side effects you have had to your study doctor right away. Your study doctor may give you other drugs to help with side effects. If you or your study doctor thinks that you cannot tolerate the side effects, the study drug may be stopped altogether and you will be withdrawn from the study.

Ask the study doctor for further information about the risks of ombitasvir/paritaprevir/ritonavir, dasabuvir and RBV.

Please tell the study doctor or study staff right away if you have any side effects. Please tell them if you have any other problems with your health or the way you feel during the study, whether or not you think these are related to the study drug.

**Reproductive Risks**

If you are a woman of childbearing potential who is sexually active with a non-vasectomized male partner, you should have been using at least one effective method of birth control at the time of screening. ~~During this trial, Y~~ you must also agree to use two effective birth control methods, as discussed with the study doctor, during the study starting with Study Day 1 and for 6 months after you stop taking the RBV.

Men who are not surgically sterile, but sexually active with female partners of childbearing potential, must also agree to use two effective birth control methods as discussed with the study doctor during the study starting with Study Day 1 and for 6 months after you stop taking the RBV.

Each of the following is considered an effective method of birth control:

- Intrauterine device (IUD)
- Condom with spermicide

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- Diaphragm with spermicide
- Cervical cap with spermicide
- Contraceptive sponge with spermicide
- Participants who are taking an ethinyl estradiol-containing medication will be asked to stop taking these medicines before starting dosing with study drugs, or switch to a different method of birth control if they are being used for birth control. Your study doctor should talk to you about this, if you are using an ethinyl estradiol-containing birth control medicine (See Section "Risk of ALT Elevations" above)

Even while using the required birth control methods, you or your partner could get pregnant during the study. It is important to tell the study doctor immediately if you or your partner become pregnant or believes that you or she could be pregnant. RBV dosing will be stopped immediately. If you are a woman and become pregnant during the dosing period, the ~~DAAs~~ **Viekira Pak** (OBV/PTV/r, DSV) may be continued at the principal investigator's discretion after discussion with you, if the benefit of continuing **Viekira Pak** ~~DAAs~~ is felt to outweigh the potential risk. **In the event that a positive result is obtained on a pregnancy test or if you become pregnant during the Treatment Period, the administration of the HCV regimen must be discontinued immediately.** If you decided to stay on study after finding out that you are pregnant, please note that the risks to you and your baby are unknown with AbbVie's **Viekira Pak** ~~DAAs~~ and you will be presented with this same informed consent form to read, sign and date again.

If you (or your partner) become pregnant, you will be encouraged to report any pregnancies that occur up to 6 months following your last dose of RBV. You will also be asked to notify the study doctor when you deliver the baby or in case you have an abortion. If you deliver the baby, you will be asked to provide the following information: date of delivery, birth weight and length, boy or girl, problems during pregnancy or delivery, and if your baby had any birth defects. The study doctor may share this information with the sponsor and ~~Quorum Review~~ **IntegReview IRB**, a group of people who review research studies to protect the rights and welfare of research participants.

For male participants: The study doctor or study staff may ask your partner for information about her pregnancy and the child's health at birth and may share this information with the sponsor.

All participants (male and female) are responsible for informing their partner(s) of these risks and for reporting any pregnancy to the study doctor.

**Allergic Reaction Risks**

Sometimes people have allergic reactions to OBV/PTV/r, dasabuvir, and ribavirin. If you have a very bad allergic reaction, you could die. Some things that happen during an allergic reaction that could be a sign or symptom of a life-threatening allergic reaction (anaphylaxis) are:

- ~~a~~**A** rash
- ~~a~~**f**Feeling of dread
- ~~h~~**H**aving a hard time breathing
- ~~w~~**W**heezing

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- ~~a-s~~ Sudden drop in blood pressure (making you feel dizzy or lightheaded)
- ~~swelling~~ Swelling around the mouth, throat, or eyes
- ~~swelling~~ Swelling of the throat
- ~~a-f~~ Fast pulse
- ~~sweating~~ Sweating
- ~~inability~~ Inability to breathe without assistance

You should get medical help and contact the study doctor or study staff if you have any of these or any other side effects during the study.

**Drug Interaction**

It is possible that taking the study drugs with your regular medications or supplements may change how the study drugs, your regular medications, or your regular supplements work. It is very important that you tell the study doctor about all medications or supplements you are taking during the study, including those you take as needed or which you take only occasionally.

**Risks Associated with Discontinuation**

Stopping the study drugs before the dosing period has been completed can reduce the chance that your HCV will be successfully cured. In addition, stopping OBV/PTV/r, dasabuvir and RBV before the dosing period has been completed might increase the chance that your HCV will develop resistance to one or all of these drugs. It is possible that virus with resistance to these drugs may also be more difficult to treat in the future with other anti HCV drugs.

**Other Risks Related to Study Procedures**

***Stopping or Changing Your Regular Medications***

If you stop or change your regular medication to be in the study, your health might get worse. Please tell the study doctor or study staff right away if you have any problems when you stop taking or change your regular medication.

**ECG Collection**

To do the ECG, you will have pads placed on different parts of your body. There is no pain or discomfort during an ECG; however, removing the pads may cause some irritation to your skin.

**Blood Draws**

The drawing of blood samples may cause bruising (black and blue marks), bleeding from the puncture site after the needle has been withdrawn, discomfort where the blood was taken, infection, formation of a blood clot or swelling of the vein and surrounding tissue and fainting.

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Fainting occasionally occurs during, or shortly after, blood is drawn; this event most frequently occurs when the subject gets up quickly from a sitting or lying down position. If you feel faint, you should notify study staff and lie down immediately to avoid possible injury caused by falling.

**Other Possible Risks**

There is a risk that your HCV may become resistant to OBV/PTV/r, dasabuvir or RBV during this study. The risk that your HCV will develop resistance is unknown. It is also not known how long HCV might remain resistant to ombitasvir/paritaprevir/ritonavir or dasabuvir after you stop taking it. Resistance to ombitasvir/paritaprevir/ritonavir, dasabuvir or ribavirin may lead to resistance to other types of anti-HCV drugs similar to the ones taken in this study, which could affect your response to treatment in the future. During the course of this study, you will be monitored for the development of resistance.

There is a risk of loss of confidentiality of your information. You will read more about the protection of your information later in this form. Please ask the study doctor or study staff if you would like to know more about how your information will be protected while you are in this study.

**Unknown Risks**

You might have side effects or discomforts that are not listed in this form, which may include your HCV infection and/or liver disease getting worse or even death. Some side effects may not be known yet. Tell the study doctor or study staff right away if you experience any side effects or discomforts.

**Costs**

Some of the study's procedures are being performed only for study purposes and others may be performed even if you are not in the study. You will not be charged for the required study drugs or for procedures that are only being done for the study. However, you will still be responsible for the cost of your standard of care medical care such as liver ultrasounds if needed. Before you agree to be in this study, you should contact your health-care payer/insurance company to see if your plan will cover the costs required as part of your participation. You can ask the study doctor or study staff to find out more about costs.

**Compensation**

You will not be paid for your participation in this study. The IRB agreed that you may be reimbursed for travel expenses for study required visits. You will only be reimbursed for actual expenses incurred up to a maximum of \$500.00. ~~If you do not complete the study, you will receive reimbursement only for the visits you have completed.~~ If you do not complete the study, you will receive reimbursement only for the visits you have completed up to a maximum of \$50.00 per visit.

**Benefits and Alternatives to Participation**

The information that is obtained during this study may be useful scientifically and thus be helpful to others requiring the same treatment.

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You may or may not receive any direct medical benefit from being in this study. Your condition may get better, it may get worse, or it may stay the same.

You do not have to participate in this study to receive treatment for your condition. There are other approved drugs available by prescription, including pegIFN and RBV. Your study doctor can discuss the risks and advantages of these alternative treatment methods with you.

**New Information**

You will be informed in writing in a timely manner and will be asked to sign a new (revised) informed consent if new information that could affect your willingness to continue participation in this study becomes available.

**In Case of Research-Related Injuries**

If, during your participation in this study, you are injured as a direct result of the study treatment, American Research Corporation agrees to pay reasonable medical expenses necessary to treat the injury, provided you have followed the directions of the study doctor and to the extent you are not otherwise reimbursed by medical insurance. If you desire, you may arrange to have treatment performed by a licensed doctor selected by you, or, upon your request, American Research Corporation will arrange to have treatment provided by the study doctor or another licensed doctor. American Research Corporation makes no commitment to provide compensation except as described above.

In the event of an emergency, seek immediate medical attention.

**Confidentiality**

A description of this clinical study will be available on <http://www.ClinicalTrials.gov>, as required by US law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

**Data We Collect From You**

Your personal health information from your original medical records and all data resulting from your participation in this research will be collected during the course of this study. Your personal health information could include physical examination details, as well as the results of any blood testing, x-rays, other medical procedures, or tissue sample testing.

**How Your Data Will Appear**

Your identity and contact details will not be disclosed unless required by law. Rather, your identity and contact details will be replaced by a code, such as a number.

**NOT TO BE USED FOR SUBJECT ENROLLMENT**

**Why We Collect These Data**

Your personal health information will be used for clinical research and may also be used for seeking approval from regulatory authorities to market the studied drugs. It may also be used in study reports or for scientific presentations, but in a way that will not identify you by name. Your personal health information will be kept confidential and, unless required by law, will not be made publicly available. After this study has been completed, it is possible that your coded health information will be used for future research.

**Who Will See Your Data**

The only people with access to your personal health information in identifiable form will be the study doctor, personnel helping study doctor conduct the study at the facility, sponsor representatives who are checking that the study is conducted properly, and regulatory authorities where required by law.

By signing this document you are allowing the study doctor and personnel at the facility of American Research Corporation and AbbVie to have access to your personal health information for the purpose of collecting data, verifying the data are correct, and checking that the study is conducted properly.

In order to complete the research, AbbVie (**the company providing the study drugs**), the study doctor and personnel at the facility, the IRB and domestic and foreign regulatory authorities responsible for overseeing research studies (including the US Food and Drug Administration [FDA], US Department of Health and Human Services, and/or equivalent government agencies in other countries) will have access to your coded health information.

Additionally, your personal health information may no longer be protected by HIPAA (Health Insurance Portability and Accountability Act) once it is disclosed to AbbVie by the study doctor. However, AbbVie will take reasonable measures to keep your personal health information confidential. Unless withdrawn, your HIPAA authorization has no expiration date, since information collected for research purposes continues to be analyzed for many years. If the results of the study are published, your identity will remain confidential.

**IntegReview IRB, and accrediting agencies may inspect and copy your records, which may have your name on them. Therefore, total confidentiality cannot be guaranteed. If the study results are presented at meetings or printed in publications, your name will not be used.**

**Taking Back Your Permission to Use or Disclose Your Personal Health Information**

To take back your permission to use or disclose your personal health information, you must write to: **Fred Poordad, MD at American Research Corporation, 607 Camden Street, Suite 101, San Antonio, TX 78215.** If you do this, you will no longer be allowed to be in this study. Any information that has already been collected at the time you take back your permission will be kept and, where the law allows, your personal health information, will continue to be used by the study doctor or AbbVie or other parties involved with the study.

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**Rights to Your Data**

You may have the right to access, correct and make a copy of your medical and/or clinical study records as allowed by applicable privacy laws. You may ask to see your records by requesting such records from the study doctor or the facility(ies) where the study is being conducted. However, to ensure the valid results of the study, you agree that you may not be able to review or make a copy of some of your records related to the study until after the study has been completed.

When you sign this document, you agree to the access, collection, processing and transfer of your personal health information as described in this informed consent document.

**CONTACT INFORMATION**

**If you have questions, concerns, or complaints about this study or to report a study related injury, contact:**

**Fred Poordad, M.D.  
210-253-3426 daytime telephone number and  
after hours number of the investigator**

**If you are unable to reach anyone at the number(s) listed above and you require immediate (life threatening) medical attention, please go to the nearest emergency room.**

**If you do not want to talk to the investigator or study staff, if you have concerns or complaints about the research, or to ask questions about your rights as a study subject you may contact IntegReview. IntegReview's policy indicates that all concerns/complaints are to be submitted in writing for review at a convened IRB meeting to:**

<b>Mailing Address:</b>	<b>OR</b>	<b>Email Address:</b>
<b>Chairperson IntegReview IRB 3815 S. Capital of Texas Highway Suite 320 Austin, Texas 78704</b>		<b><u><a href="mailto:integreview@integreview.com">integreview@integreview.com</a></u></b>

**If you are unable to provide your concerns/complaints in writing or if this is an emergency situation regarding subject safety, contact our office at:**

**512-326-3001 or  
toll free at 1-877-562-1589  
between 8 a.m. and 5 p.m. Central Time**

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**IntegReview has approved the information in this consent form and has given approval for the investigator to do the study. This does not mean IntegReview has approved your being in the study. You must consider the information in this consent form for yourself and decide if you want to be in this study.**

**Withdrawal/Voluntary Participation**

Participation in this study is voluntary. You can stop participating in the study at any time. If you decide not to participate in the study or to withdraw from the study, the quality of your medical care or any benefits to which you are otherwise entitled will not be affected. Your study doctor may also end your participation in the study if he/she believes that it is in your best interest or if you are unable to follow the requirements of the study.

When you withdraw from the study for any reason, all study drugs and study drug containers including those unused and empty must be returned to the study site. You will also be asked to return to the site so that the study doctor may perform a final evaluation, which may include a physical examination and/or laboratory tests.

**THE REASON FOR INSTITUTIONAL REVIEW BOARDS AND INFORMED CONSENT**

*What is a consent form?*

The informed consent document contains information required by federal regulations. The informed consent document must be approved by an Institutional Review Board (IRB).

*What is an Institutional Review Board (IRB)?*

An Institutional Review Board (IRB) is a group of people that reviews research studies. The main goal of this review is to protect the rights and well being of the human subjects participating in research studies.

IntegReview, the IRB for this study

IntegReview is an IRB whose board members provide IRB services across the United States, Canada, Latin America and Japan.

To meet requirements of the law, the IntegReview Boards currently include:

- Doctors
- Pharmacists
- Nurses
- Toxicologists (people who study the harmful effects of chemicals)
- Other specialists
- Others who do not have a background in science/medicine

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**Consent**

I have read and understand this consent form and its contents were explained. My questions have been answered to my satisfaction. I consent voluntarily to participate in this research study and I will receive a signed and dated copy of this consent form for my records. By signing this consent form, I am not giving up any of my legal rights.

By signing this informed consent form, I am authorizing access, use and transfer of my personal data as described elsewhere in this consent.

\_\_\_\_\_  
\_\_\_\_\_  
~~Name of Subject (Printed)~~\_\_\_\_\_

\_\_\_\_\_  
\_\_\_\_\_  
~~Signature of Subject~~\_\_\_\_\_ ~~Date~~

\_\_\_\_\_  
\_\_\_\_\_  
~~Name of Person Conducting~~  
~~Informed Consent Discussion (Printed)~~\_\_\_\_\_

\_\_\_\_\_  
\_\_\_\_\_  
~~Signature of Person Conducting~~  
~~Informed Consent Discussion~~\_\_\_\_\_ ~~Date~~

\_\_\_\_\_  
**Printed Name of Adult Study Subject**

\_\_\_\_\_  
**Signature of Adult Study Subject** **Date**

\_\_\_\_\_  
**Printed Name of Person Explaining Consent Form**

\_\_\_\_\_  
**Signature of Person Explaining Consent Form** **Date**

**You will be given a signed and dated copy of this informed consent to keep.**

**APPROVED BY  
INTEGREVIEW IRB  
MARCH 17, 2016**

**RESEARCH SUBJECT INFORMATION AND CONSENT FORM  
AGREEMENT TO BE IN A RESEARCH STUDY**

**NAME OF SPONSOR COMPANY:** American Research Corporation at the Texas Liver Institute

**NUMBER AND NAME OF STUDY:** TLI\_IIS\_01\_2015; "A STUDY TO INVESTIGATE HCV RESPONSE RATES IN REAL WORLD PATIENTS TRADITIONALLY EXCLUDED FROM CLINICAL TRIALS: THE HEARTLAND STUDY"

**NAME OF PERSON IN CHARGE OF THE  
RESEARCH STUDY**

**(INVESTIGATOR/STUDY DOCTOR):** Fred Poordad, M.D.

**DAYTIME AND AFTER HOURS TELEPHONE:** 210-253-3426

Before you can make an informed decision to participate in this research study, you should understand the possible risks and benefits of this study. This process is known as informed consent. This consent form contains information about the study and has been reviewed and approved by the IRB, a group of independent experts and lay persons. This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision. If you decide to participate in this study, you will be asked to read and sign this consent form to confirm that you have had the study explained to you, and you have agreed to participate. You will receive a copy of the signed and dated consent form.

**Introduction**

You are being asked to participate in this research study of FDA approved drugs, VIEKIRA PAK (Paritaprevir/Ritonavir/Ombitasvir tablets; Dasabuvir tablets) and Ribavirin tablets. You are being asked because you have been diagnosed with the chronic genotype 1 hepatitis C virus (HCV) infection and are with or without a diagnosis of compensated cirrhosis (early liver damage in which the body functions normally despite the damaged liver tissue) and either you have not taken medications to treat the HCV infection or you have been previously treated for HCV infection and have failed a regimen including pegIFN/RBV +/- telaprevir, boceprevir, or simeprevir.

The FDA approved VIEKIRA PAK (ombitasvir, paritaprevir, ritonavir fixed dose combination tablets copackaged with dasabuvir tablets) for use with or without ribavirin for the treatment of patients with genotype 1 chronic hepatitis C virus (HCV) infection.

Ombitasvir (OBV), ritonavir (r) and Paritaprevir (PTV) will be combined into one pill, known as OBV/PTV/r. This combination pill will be packaged with Dasabuvir to make the VIEKIRA PAK. In addition to VIEKIRA PAK, you will also receive ribavirin (RBV). Ribavirin is also approved by the FDA for the treatment of chronic HCV in adults. The RBV dose will be given at an investigational dose. "Investigational" means the the dose being given has not been approved by the United States Food and Drug Administration. These drugs are intended to prevent the HCV from multiplying in the human body.

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Be aware that this form refers to OBV/PTV/r, DSV, and RBV as “study drug.”

American Research Corporation is sponsoring this study. Any reference to "American Research Corporation" or "sponsor" in this consent form also means any company that might take over American Research Corporation's interests as sponsor of the study, whether before or after the completion of the study. American Research Corporation is paying the study doctor to perform this study.

Being in this study does not replace your regular medical care.

You must be honest with the investigator about your health history or you may harm yourself by participating in this study.

**Purpose of the Study**

The purpose of this study is to see if the study drugs are safe and able to reduce the amount of HCV in your blood.

**Study Information**

This study is being conducted as a single center study at American Research Corporation in San Antonio and 2 satellite sites located in Austin and McAllen Texas. This study is designed to enroll approximately 100 men and women ages 18 years and older.

This is an open-label study. This means that you, your doctor/study staff and the study sponsor will know which drugs you will be receiving.

The study consists of 2 parts: Treatment Period and Post Treatment Period

**Part 1: Treatment Period**

You will be assigned to one of the following groups based on the current guidance of the Viekira Pak insert. You will either be in the 12-week treatment arm or the 24-week treatment arm as described below.

**12-Week Treatment Arm:**

- To include patients with Genotype 1a without cirrhosis, Genotype 1b with cirrhosis.
- VIEKIRA PAK taken by mouth for 12 weeks
- RBV according to package insert:
  - if you weigh less than 165 lbs (75 kg), you will take 1000 mg daily (e.g., two 200 mg capsules in the morning and three 200 mg capsules in the evening) by mouth for 12 weeks
  - if you weigh 165 lbs (75 kg) or more, you will take 1200 mg daily (e.g., three 200 mg capsules twice daily) by mouth for 12 weeks

**12-Week Treatment Arm:**

- To include patients with Genotype 1b without cirrhosis.
- VIEKIRA PAK taken by mouth for 12 weeks

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**24-Week Treatment Arm:**

- To include patients with Genotype 1a with cirrhosis.
- VIEKIRA PAK taken by mouth for 24 weeks
- RBV:
  - if you weigh less than 165 lbs (75 kg), you will take 1000 mg daily (e.g., two 200 mg capsules in the morning and three 200 mg capsules in the evening) by mouth for 24 weeks
  - if you weigh 165 lbs (75 kg) or more, you will take 1200 mg daily (e.g., three 200 mg capsules twice daily) by mouth for 24 weeks.

**Part 2 Post Treatment Period**

After completing Part 1, you will be monitored for an additional 12 weeks following the last dose of study drugs to see if the hepatitis C virus can still be detected, and if so, whether it has become resistant to any of the study drugs. Resistant means that the drugs are no longer working against the virus.

**Study Duration**

Your participation in this study will last approximately 24 to 36 weeks (excluding the screening period) dependent upon your treatment assignment. You may need to visit the research center for up to 10 study visits.

**Study Procedures**

If you agree to be in this study, you will undergo some activities, tests and evaluations to determine if you are eligible for this study. Such tests and evaluations listed in the table below are completed during a screening period that takes place before study participation. If you are eligible to participate in this study, you will undergo the other procedures listed in the table below.

**Study Activities**

Activity									
	Treatment Visits – All Patients					Treatment Visits Patients Requiring 24 Week Treatment			Premature D/C During Treatment Period
	Screening	Day1/ Baseline	Week 4	Week 8	Week 12 (EOT)	Week 16	Week 20	Week 24 (EOT)	
Informed Consent	X								
Medical History	X	X							
Physical Exam*	X	X			X			X	X
12 Lead ECG*	X	X			X			X	X
Vital Signs	X	X	X	X	X	X	X	X	X

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Blood and Urine for lab tests	X	X	X	X	X	X	X	X	X
Pregnancy Test [blood (b), urine (u)]	X (b)	X (u, b)	X (u)	X (u)	X (u)	X (u)	X (u)	X (u)	X (u)
Drug Screen (urine)	X	X							
AFP Test	X								
HbsAg/HCV-ab/HIV	X								
HCV Genotype Blood Test	X								
HCV RNA PCR	X	X	X	X	X	X	X	X	X
HCV Resistance Sample (baseline for all; only when detectable HCV RNA during treatment after previously testing negative)		X							
Concomitant Medication Assessment	X	X	X	X	X	X	X	X	X
Randomization		X							
SF36v2 survey (only at baseline and EOT for all patients)		X			X * *			X * *	X * *
Side effects Assessment			X	X	X	X	X	X	X
Study Drugs Dispensed		X	X	X	X	X	X		

\*Physical exam and 12 Lead ECG will be performed on all patients at screening, baseline and end of treatment (either Week 12, Week 24 or Early Discontinuation)

\*\*Performed twice for all patients: baseline and EOT (week 12 or week 24 or early discontinuation)

Wk = Week; EOT = End of Treatment; D/C = Discontinuation; PTW = Post-Treatment Week; PT D/C = Post-Treatment Discontinuation

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If you are enrolled in 12 week treatment arm you will complete all specified study activities up to 12 weeks. If you are enrolled in 24 week treatment arm you will complete all specified study activities up to 24 weeks.

Note: At every study visit, you will be asked about any change in the medications you are taking, any problems you are having, and any side effects you are experiencing, which may or may not be related to the study or whether you have made any visits to other doctors or hospitals.

**Study Activities (Continued)**

<b>Activity</b>	<b>Post Treatment Week 4</b>	<b>Post Treatment Week 12 or Early PT D/C</b>
Physical Exam	X	X
Vital signs	X	X
Side effects Assessment	X	X*
HCV RNA	X	X
HCV Resistance Sample (for those with detectable HCV RNA)*		Only in non-SVR patients

\*Only for early post-treatment discontinuations. Side effect assessment only assessed up to 30 days post-treatment.

**Blood Draws**

The blood samples will be taken by individual needle sticks into one of your arm veins.

You will undergo approximately 10-11 blood draws during the course of this study. The maximum amount of blood taken for the entire study for 12 week treatment period will be approximately 133 mL. If you are in the 24 week treatment group it is approximately 193 mL.

**HIV AND HEPATITIS**

If any person is exposed to your blood, you must have your blood tested for the hepatitis viruses and for HIV. HIV is the virus that causes AIDS.

If the HIV test is positive, a follow-up test will be done. If the follow-up test is also positive, you will be told in private and you will also be told about counseling.

It may take weeks or months after being infected with HIV for the test to be positive. The HIV test is not always right.

Positive test results may be required to be reported to the State Department of Health. If you have any questions about what information is required to be reported please ask the investigator or study staff.

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Although this testing is supposed to be private, this cannot be guaranteed. For example, it is possible for a court of law to get health or study records without your permission.

**Additional Procedure Information**

- Pregnancy testing: The study doctor or study staff will tell you if the pregnancy test results are positive. The results of the pregnancy testing must be negative in order for you to be in the study.

**Subject's Responsibilities**

In order for this study to provide good information about how this drug works in subjects with HCV, you will be expected to do the following:

- Follow the instructions of your study doctor.
- Come to all your scheduled study visits and procedures.
- Certain medications you are taking or have taken in the past may keep you from being in this study. You may be required to stop or adjust the dose for certain medications and supplements you are currently taking either prior to starting study drugs or during the study. Please review all of your medications with your study doctor.
- Do not change any of your other medications or start any new medications without checking with your study doctor as certain medications could interact with the study drugs.
- Tell the study staff what procedures/conditions you have had in the past as they may keep you from being in this study.
- Fill out your health-based questionnaires completely and honestly. You will be given one questionnaire at two time points throughout the study to assess what you think of your health and quality of life.
- If you see a doctor outside the research study, tell the doctor you are in an investigational research study as certain medications could interact with the study drugs.
- Tell the study staff about any health problems you are having even if you don't think they are important.
- Tell the study staff if you wish to stop being in the study and come back for the final visit.
- Do not participate in any other studies during your participation in this study.
- At every study visit, you will be asked to provide any changes in the medications you are taking, any problems you are having, and any side effects you are experiencing, which may or may not be related to the study or whether you have made any visits to other doctors or hospitals.

**Study Drug Instructions**

You will receive specific instructions on how to take all of the study drugs in this study. You will have a discussion with your study doctor or study staff about the importance of taking your study drugs at the time and at the dose that your study doctor has instructed. Should you miss taking a dose at a scheduled time, it is important that you tell your study doctor at your next visit. If you decide to stop taking your study drugs, it is very important that you tell your study doctor right away.

- Take and store your study drug as instructed and return the unused study drug and/or empty containers to the study doctor's office at each visit.
- Do not share your study drug with anyone. You are the only person allowed to take the study drug.

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- Keep the study drug and study supplies out of the reach of children and persons of limited ability to read or understand.

**Risks and Discomforts**

If you do not understand what any of these side effects mean, please ask the study doctor or study staff to explain these terms to you.

You must tell the investigator or study staff about all side effects that you have. If you are not honest about your side effects, you may harm yourself by staying in this study.

When you take more than one drug at a time, the side effects can be worse or different than if you take either drug by itself.

Until you know how the drugs will affect you, you should use caution by avoiding stairs, not driving a car or working with machinery.

The most common side effects seen in healthy volunteers taking multiple doses of paritaprevir, ombitasvir, and dasabuvir given together were:

- Headache: 7.3%, about 7 in 100 subjects
- Diarrhea: 3.6%, about 4 in 100 subjects
- Nausea: 2.9%, about 3 in 100 subjects
- Dizziness: 2.9%, about 3 in 100 subjects
- Constipation: 2.5%, about 3 in 100 subjects
- Common cold symptoms: 2.2%, about 2 in 100 subjects

**HCV-infected people receiving similar drug combinations in clinical trials experienced:**

- Tiredness (34.2%, about 34 in 100 people)
- Nausea (22.3%, about 22 in 100 people)
- Itching (15.7%, about 16 in 100 people)
- Trouble sleeping (14.0%, about 14 in 100 people)
- Weakness (13.5%, about 14 in 100 people)
- Low blood count (5.3%, about 5 in 100 people)

Risk of liver problems and failure:

A small number of participants have experienced severe liver problems while on the Viekira Pak, some of whom died or required liver transplantation. These liver problems included confusion, abdominal fluid accumulation and swelling, bleeding, and changes in blood tests that measure the function of the liver.

It is unknown whether or not these liver problems were directly caused by the Viekira Pak or just as a result of their advanced liver disease. Most participants who died or needed a liver transplant already had advanced disease before starting the Viekira Pak. Blood tests that measure your liver function will be performed during the study, and your study doctor will monitor you for signs of severe liver problems. Let your study doctor know if you have swelling of the stomach area, bleeding, or are feeling confused.

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**Risk of ALT elevations:**

About 1 in 100 participants (1%) receiving Viekira Pak experienced an increase in ALT (a blood test that increases when your liver is inflamed) levels. Increased levels of ALT happened more often in people receiving medicines containing ethinyl estradiol, which many birth control pills contain. These increased ALT levels did not cause symptoms, usually happened during the first 4 weeks of dosing, and got better with continued dosing with the Viekira Pak.

Participants who are taking ethinyl estradiol-containing medicines will be asked to stop taking these medicines before starting dosing with the Viekira Pak. Ethinyl estradiol-containing medicines include pills, patches, or rings that deliver ethinyl estradiol for the purpose of contraception or for other clinical indications, including some hormone replacement therapy. Estrogens used to treat symptoms of menopause like vaginal creams do not typically contain ethinyl estradiol. If you are using an estrogen, it is important for your study doctor to check what type of estrogen it contains.

If you are taking an ethinyl estradiol containing medication for birth control, your study doctor may switch you to a different method of birth control (for example, a progestin-only containing contraceptive or non-hormonal form of birth control). You may restart your ethinyl estradiol-containing medicine about 2 weeks after your study drug dosing is completed. Your blood levels of ALT will be measured during this study. Let your study doctor know if you have new onset of:

- Fatigue
- Weakness
- Lack of appetite
- Nausea and vomiting
- Jaundice

**General Information**

The study medications may interfere/interact with some medications, so you must let your doctor know about any medications, herbals or vitamins that you are taking.

**Increased bilirubin levels**

Some people taking the Viekira Pak, especially those who were also taking ribavirin or the HIV medicine atazanavir, had increased levels of bilirubin (a substance measured in your blood that is produced when red blood cells are broken down) which can cause yellowing in the eyes or under the tongue in some people. These bilirubin increases may be temporary and may not be associated with damage to the liver. Increases in bilirubin usually reach their highest level in the first week after starting the Viekira Pak, and get better with continued study drug dosing.

In some cases, increases in bilirubin can get worse. If bilirubin increase occurs with other signs such as swelling of the stomach area, vomiting of blood, or confusion, it may be a sign of a severe liver problem.

**Hemoglobin decreases**

Ribavirin (RBV) is known to cause anemia (low hemoglobin levels from having low red blood cell counts). See RBV-related risks. In studies where participants received the Viekira Pak with RBV, hemoglobin levels decreased during dosing and got better after dosing was finished. Low hemoglobin

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levels were usually treated by decreasing the dose of RBV given. Participants rarely required blood transfusions or other medicines to increase hemoglobin levels.

**General Information**

The study drugs may interfere/interact with some medications. If you take a calcium channel blocker, you may experience leg swelling after starting the study drugs.

Some drug interactions may be serious or life threatening. You must let your study doctor know about any medications or vaccines (oral, inhaled, topical, or other), including herbals or vitamins that you are taking.

It is important to remember that the recently approved Viekira Pak is still being studied in humans, so some of the risks of the combinations of these drugs are not yet known.

**Information about pregnancy**

Some drugs cause premature (early) birth or birth defects. The risks of the study drugs in pregnancy are not known. However, RBV is known to cause birth defects and can lead to the death of an unborn child - see RBV related risks.

**Ribavirin Study Drug Risks**

Ribavirin has been marketed for HCV infection administered in combination with other HCV drugs (ribavirin is not effective against HCV infection when given by itself). Side effects which may be experienced with RBV include:

- Nausea
- Anorexia
- Vomiting
- Diarrhea
- Dyspepsia (stomach upset)
- Abdominal pain
- Insomnia
- Rash
- Hemolytic anemia (decreases in your red blood cells caused by breakdown of your red blood cells). The breakdown of red cells may lead to increased levels of bilirubin, and uric acid (these will show up in lab results). The hemolytic anemia may cause worsening of heart disease which may lead to heart attacks and, sometimes, death.
- Significant birth defects if pregnancy occurs while taking ribavirin or if pregnancy occurs up to 6 months after taking ribavirin.

You should not use ribavirin if you have been diagnosed with blood disorders such as sickle cell anemia or certain other genetic blood disorders which affect your red cells.

If you (or your partner if you are a male study subject) become pregnant or breastfeed during the study while receiving ribavirin, or for 6 months after having received ribavirin, it can have harmful effects on fetal development. Because there is a potential risk of fetal death or injury, you should not plan a

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pregnancy, or breastfeed if you are a female subject or a female partner of a male subject, during the trial and for a minimum of 6 months after the last dose of ribavirin.

You should get medical help and contact the study doctor or study staff if you have any of these or any other side effects during the study.

It is important to remember that some the risks of ribavirin may not be fully known.

The information provided here only describes some of the side effects reported with RBV. Therefore, you should refer to RBV label for additional risks.

Your study doctor will be monitoring you for side effects from ombitasvir/paritaprevir/ritonavir, dasabuvir and RBV. It is important that you report any side effects you have had to your study doctor right away. Your study doctor may give you other drugs to help with side effects. If you or your study doctor thinks that you cannot tolerate the side effects, the study drug may be stopped altogether and you will be withdrawn from the study.

Ask the study doctor for further information about the risks of ombitasvir/paritaprevir/ritonavir, dasabuvir and RBV.

Please tell the study doctor or study staff right away if you have any side effects. Please tell them if you have any other problems with your health or the way you feel during the study, whether or not you think these are related to the study drug.

**Reproductive Risks**

If you are a woman of childbearing potential who is sexually active with a non-vasectomized male partner, you should have been using at least one effective method of birth control at the time of screening. You must also agree to use two effective birth control methods, as discussed with the study doctor, during the study starting with Study Day 1 and for 6 months after you stop taking the RBV.

Men who are not surgically sterile, but sexually active with female partners of childbearing potential, must also agree to use two effective birth control methods as discussed with the study doctor during the study starting with Study Day 1 and for 6 months after you stop taking the RBV.

Each of the following is considered an effective method of birth control:

- Intrauterine device (IUD)
- Condom with spermicide
- Diaphragm with spermicide
- Cervical cap with spermicide
- Contraceptive sponge with spermicide
- Participants who are taking an ethinyl estradiol-containing medication will be asked to stop taking these medicines before starting dosing with study drugs, or switch to a different method of birth control if they are being used for birth control. Your study doctor should talk to you about this, if you are using an ethinyl estradiol-containing birth control medicine (See Section "Risk of ALT Elevations" above)

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Even while using the required birth control methods, you or your partner could get pregnant during the study. It is important to tell the study doctor immediately if you or your partner become pregnant or believes that you or she could be pregnant. RBV dosing will be stopped immediately. If you are a woman and become pregnant during the dosing period, the Viekira Pak (OBV/PTV/r, DSV) may be continued at the principal investigator's discretion after discussion with you, if the benefit of continuing Viekira Pak is felt to outweigh the potential risk. **In the event that a positive result is obtained on a pregnancy test or if you become pregnant during the Treatment Period, the administration of the HCV regimen must be discontinued immediately.** If you decided to stay on study after finding out that you are pregnant, please note that the risks to you and your baby are unknown with AbbVie's Viekira Pak and you will be presented with this same informed consent form to read, sign and date again.

If you (or your partner) become pregnant, you will be encouraged to report any pregnancies that occur up to 6 months following your last dose of RBV. You will also be asked to notify the study doctor when you deliver the baby or in case you have an abortion. If you deliver the baby, you will be asked to provide the following information: date of delivery, birth weight and length, boy or girl, problems during pregnancy or delivery, and if your baby had any birth defects. The study doctor may share this information with the sponsor and IntegReview IRB, a group of people who review research studies to protect the rights and welfare of research participants.

For male participants: The study doctor or study staff may ask your partner for information about her pregnancy and the child's health at birth and may share this information with the sponsor.

All participants (male and female) are responsible for informing their partner(s) of these risks and for reporting any pregnancy to the study doctor.

**Allergic Reaction Risks**

Sometimes people have allergic reactions to OBV/PTV/r, dasabuvir, and ribavirin. If you have a very bad allergic reaction, you could die. Some things that happen during an allergic reaction that could be a sign or symptom of a life-threatening allergic reaction (anaphylaxis) are:

- A rash
- Feeling of dread
- Having a hard time breathing
- Wheezing
- Sudden drop in blood pressure (making you feel dizzy or lightheaded)
- Swelling around the mouth, throat, or eyes
- Swelling of the throat
- Fast pulse
- Sweating
- Inability to breathe without assistance

You should get medical help and contact the study doctor or study staff if you have any of these or any other side effects during the study.

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**Drug Interaction**

It is possible that taking the study drugs with your regular medications or supplements may change how the study drugs, your regular medications, or your regular supplements work. It is very important that you tell the study doctor about all medications or supplements you are taking during the study, including those you take as needed or which you take only occasionally.

**Risks Associated with Discontinuation**

Stopping the study drugs before the dosing period has been completed can reduce the chance that your HCV will be successfully cured. In addition, stopping OBV/PTV/r, dasabuvir and RBV before the dosing period has been completed might increase the chance that your HCV will develop resistance to one or all of these drugs. It is possible that virus with resistance to these drugs may also be more difficult to treat in the future with other anti HCV drugs.

**Other Risks Related to Study Procedures**

***Stopping or Changing Your Regular Medications***

If you stop or change your regular medication to be in the study, your health might get worse. Please tell the study doctor or study staff right away if you have any problems when you stop taking or change your regular medication.

**ECG Collection**

To do the ECG, you will have pads placed on different parts of your body. There is no pain or discomfort during an ECG; however, removing the pads may cause some irritation to your skin.

**Blood Draws**

The drawing of blood samples may cause bruising (black and blue marks), bleeding from the puncture site after the needle has been withdrawn, discomfort where the blood was taken, infection, formation of a blood clot or swelling of the vein and surrounding tissue and fainting.

Fainting occasionally occurs during, or shortly after, blood is drawn; this event most frequently occurs when the subject gets up quickly from a sitting or lying down position. If you feel faint, you should notify study staff and lie down immediately to avoid possible injury caused by falling.

**Other Possible Risks**

There is a risk that your HCV may become resistant to OBV/PTV/r, dasabuvir or RBV during this study. The risk that your HCV will develop resistance is unknown. It is also not known how long HCV might remain resistant to ombitasvir/paritaprevir/ritonavir or dasabuvir after you stop taking it. Resistance to ombitasvir/paritaprevir/ritonavir, dasabuvir or ribavirin may lead to resistance to other types of anti-HCV drugs similar to the ones taken in this study, which could affect your response to treatment in the future. During the course of this study, you will be monitored for the development of resistance.

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There is a risk of loss of confidentiality of your information. You will read more about the protection of your information later in this form. Please ask the study doctor or study staff if you would like to know more about how your information will be protected while you are in this study.

**Unknown Risks**

You might have side effects or discomforts that are not listed in this form, which may include your HCV infection and/or liver disease getting worse or even death. Some side effects may not be known yet. Tell the study doctor or study staff right away if you experience any side effects or discomforts.

**Costs**

Some of the study's procedures are being performed only for study purposes and others may be performed even if you are not in the study. You will not be charged for the required study drugs or for procedures that are only being done for the study. However, you will still be responsible for the cost of your standard of care medical care such as liver ultrasounds if needed. Before you agree to be in this study, you should contact your health-care payer/insurance company to see if your plan will cover the costs required as part of your participation. You can ask the study doctor or study staff to find out more about costs.

**Compensation**

You will not be paid for your participation in this study. The IRB agreed that you may be reimbursed for travel expenses for study required visits. You will only be reimbursed for actual expenses incurred up to a maximum of \$500.00. If you do not complete the study, you will receive reimbursement only for the visits you have completed up to a maximum of \$50.00 per visit.

**Benefits and Alternatives to Participation**

The information that is obtained during this study may be useful scientifically and thus be helpful to others requiring the same treatment.

You may or may not receive any direct medical benefit from being in this study. Your condition may get better, it may get worse, or it may stay the same.

You do not have to participate in this study to receive treatment for your condition. There are other approved drugs available by prescription, including pegIFN and RBV. Your study doctor can discuss the risks and advantages of these alternative treatment methods with you.

**New Information**

You will be informed in writing in a timely manner and will be asked to sign a new (revised) informed consent if new information that could affect your willingness to continue participation in this study becomes available.

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**In Case of Research-Related Injuries**

If, during your participation in this study, you are injured as a direct result of the study treatment, American Research Corporation agrees to pay reasonable medical expenses necessary to treat the injury, provided you have followed the directions of the study doctor and to the extent you are not otherwise reimbursed by medical insurance. If you desire, you may arrange to have treatment performed by a licensed doctor selected by you, or, upon your request, American Research Corporation will arrange to have treatment provided by the study doctor or another licensed doctor. American Research Corporation makes no commitment to provide compensation except as described above.

In the event of an emergency, seek immediate medical attention.

**Confidentiality**

A description of this clinical study will be available on <http://www.ClinicalTrials.gov>, as required by US law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

**Data We Collect From You**

Your personal health information from your original medical records and all data resulting from your participation in this research will be collected during the course of this study. Your personal health information could include physical examination details, as well as the results of any blood testing, x-rays, other medical procedures, or tissue sample testing.

**How Your Data Will Appear**

Your identity and contact details will not be disclosed unless required by law. Rather, your identity and contact details will be replaced by a code, such as a number.

**Why We Collect These Data**

Your personal health information will be used for clinical research and may also be used for seeking approval from regulatory authorities to market the studied drugs. It may also be used in study reports or for scientific presentations, but in a way that will not identify you by name. Your personal health information will be kept confidential and, unless required by law, will not be made publicly available. After this study has been completed, it is possible that your coded health information will be used for future research.

**Who Will See Your Data**

The only people with access to your personal health information in identifiable form will be the study doctor, personnel helping study doctor conduct the study at the facility, sponsor representatives who are checking that the study is conducted properly, and regulatory authorities where required by law.

By signing this document you are allowing the study doctor and personnel at the facility of American Research Corporation and AbbVie to have access to your personal health information for the purpose of collecting data, verifying the data are correct, and checking that the study is conducted properly.

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In order to complete the research, AbbVie (the company providing the study drugs), the study doctor and personnel at the facility, the IRB and domestic and foreign regulatory authorities responsible for overseeing research studies (including the US Food and Drug Administration [FDA], US Department of Health and Human Services, and/or equivalent government agencies in other countries) will have access to your coded health information.

Additionally, your personal health information may no longer be protected by HIPAA (Health Insurance Portability and Accountability Act) once it is disclosed to AbbVie by the study doctor. However, AbbVie will take reasonable measures to keep your personal health information confidential. Unless withdrawn, your HIPAA authorization has no expiration date, since information collected for research purposes continues to be analyzed for many years. If the results of the study are published, your identity will remain confidential.

IntegReview IRB, and accrediting agencies may inspect and copy your records, which may have your name on them. Therefore, total confidentiality cannot be guaranteed. If the study results are presented at meetings or printed in publications, your name will not be used.

**Taking Back Your Permission to Use or Disclose Your Personal Health Information**

To take back your permission to use or disclose your personal health information, you must write to: **Fred Poordad, M.D. at American Research Corporation, 607 Camden Street, Suite 101, San Antonio, TX 78215.** If you do this, you will no longer be allowed to be in this study. Any information that has already been collected at the time you take back your permission will be kept and, where the law allows, your personal health information, will continue to be used by the study doctor or AbbVie or other parties involved with the study.

**Rights to Your Data**

You may have the right to access, correct and make a copy of your medical and/or clinical study records as allowed by applicable privacy laws. You may ask to see your records by requesting such records from the study doctor or the facility(ies) where the study is being conducted. However, to ensure the valid results of the study, you agree that you may not be able to review or make a copy of some of your records related to the study until after the study has been completed.

When you sign this document, you agree to the access, collection, processing and transfer of your personal health information as described in this informed consent document.

**CONTACT INFORMATION**

If you have questions, concerns, or complaints about this study or to report a study related injury, contact:

Fred Poordad, M.D.  
210-253-3426 daytime telephone number and  
after hours number of the investigator

**If you are unable to reach anyone at the number(s) listed above and you require immediate (life threatening) medical attention, please go to the nearest emergency room.**

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If you do not want to talk to the investigator or study staff, if you have concerns or complaints about the research, or to ask questions about your rights as a study subject you may contact IntegReview. IntegReview's policy indicates that all concerns/complaints are to be submitted in writing for review at a convened IRB meeting to:

<b>Mailing Address:</b>	<b>OR</b>	<b>Email Address:</b>
Chairperson IntegReview IRB 3815 S. Capital of Texas Highway Suite 320 Austin, Texas 78704		<a href="mailto:integreview@integreview.com">integreview@integreview.com</a>

If you are unable to provide your concerns/complaints in writing or if this is an emergency situation regarding subject safety, contact our office at:

512-326-3001 or  
toll free at 1-877-562-1589  
between 8 a.m. and 5 p.m. Central Time

IntegReview has approved the information in this consent form and has given approval for the investigator to do the study. This does not mean IntegReview has approved your being in the study. You must consider the information in this consent form for yourself and decide if you want to be in this study.

**Withdrawal/Voluntary Participation**

Participation in this study is voluntary. You can stop participating in the study at any time. If you decide not to participate in the study or to withdraw from the study, the quality of your medical care or any benefits to which you are otherwise entitled will not be affected. Your study doctor may also end your participation in the study if he/she believes that it is in your best interest or if you are unable to follow the requirements of the study.

When you withdraw from the study for any reason, all study drugs and study drug containers including those unused and empty must be returned to the study site. You will also be asked to return to the site so that the study doctor may perform a final evaluation, which may include a physical examination and/or laboratory tests.

**THE REASON FOR INSTITUTIONAL REVIEW BOARDS AND INFORMED CONSENT**

***What is a consent form?***

The informed consent document contains information required by federal regulations. The informed consent document must be approved by an Institutional Review Board (IRB).

***What is an Institutional Review Board (IRB)?***

An Institutional Review Board (IRB) is a group of people that reviews research studies. The main goal of this review is to protect the rights and well being of the human subjects participating in research studies.

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**APPROVED BY  
INTEGREVIEW IRB  
MARCH 17, 2016**

***IntegReview, the IRB for this study***

IntegReview is an IRB whose board members provide IRB services across the United States, Canada, Latin America and Japan.

To meet requirements of the law, the IntegReview Boards currently include:

- Doctors
- Pharmacists
- Nurses
- Toxicologists (people who study the harmful effects of chemicals)
- Other specialists
- Others who do not have a background in science/medicine

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**Consent**

I have read and understand this consent form and its contents were explained. My questions have been answered to my satisfaction. I consent voluntarily to participate in this research study and I will receive a signed and dated copy of this consent form for my records. By signing this consent form, I am not giving up any of my legal rights.

By signing this informed consent form, I am authorizing access, use and transfer of my personal data as described elsewhere in this consent.

\_\_\_\_\_  
Printed Name of Adult Study Subject

\_\_\_\_\_  
Signature of Adult Study Subject

\_\_\_\_\_  
Date

\_\_\_\_\_  
Printed Name of Person Explaining Consent Form

\_\_\_\_\_  
Signature of Person Explaining Consent Form

\_\_\_\_\_  
Date

You will be given a signed and dated copy of this informed consent to keep.

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# Your Health and Well-Being

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APPROVED  
MARCH 17, 2016  
INTEGREVIEW

**This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. *Thank you for completing this survey!***

**For each of the following questions, please mark an ☒ in the one box that best describes your answer.**

**1. In general, would you say your health is:**

Excellent	Very good	Good	Fair	Poor
▼	▼	▼	▼	▼
<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

**2. Compared to one year ago, how would you rate your health in general now?**

Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago
▼	▼	▼	▼	▼
<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, limited a lot ▼	Yes, limited a little ▼	No, not limited at all ▼
a <u>Vigorous activities</u> , such as running, lifting heavy objects, participating in strenuous sports .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
b <u>Moderate activities</u> , such as moving a table, pushing a vacuum cleaner, bowling, or playing golf.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
c Lifting or carrying groceries .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
d Climbing <u>several</u> flights of stairs .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
e Climbing <u>one</u> flight of stairs .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
f Bending, kneeling, or stooping .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
g Walking <u>more than a mile</u> .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
h Walking <u>several hundred yards</u> .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
i Walking <u>one hundred yards</u> .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
j Bathing or dressing yourself .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3

**4. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?**

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Cut down on the <u>amount of time</u> you spent on work or other activities.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
b <u>Accomplished less</u> than you would like .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
c Were limited in the <u>kind of</u> work or other activities .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
d Had <u>difficulty</u> performing the work or other activities (for example, it took extra effort) .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

**5. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?**

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Cut down on the <u>amount of time</u> you spent on work or other activities.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
b <u>Accomplished less</u> than you would like .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
c Did work or other activities <u>less carefully than usual</u> .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

Not at all	Slightly	Moderately	Quite a bit	Extremely
▼	▼	▼	▼	▼
<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

7. How much bodily pain have you had during the past 4 weeks?

None	Very mild	Mild	Moderate	Severe	Very severe
▼	▼	▼	▼	▼	▼
<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/> 6

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a bit	Extremely
▼	▼	▼	▼	▼
<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5



9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks...

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Did you feel full of life? .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
b Have you been very nervous? .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
c Have you felt so down in the dumps that nothing could cheer you up? .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
d Have you felt calm and peaceful? .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
e Did you have a lot of energy? .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
f Have you felt downhearted and depressed? .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
g Did you feel worn out? .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
h Have you been happy? .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
i Did you feel tired? .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

**11. How TRUE or FALSE is each of the following statements for you?**

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a I seem to get sick a little easier than other people .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
b I am as healthy as anybody I know.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
c I expect my health to get worse.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
d My health is excellent.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

***Thank you for completing these questions!***



**MEMBERSHIP ROSTER**  
**As of October 1, 2015**

<b>Sponsor Name:</b> American Research Corporation at Texas Liver Institute	<b>Protocol Number:</b> TLI_IIS_01_2015
<b>Principal Investigator Name:</b> Fred Poordad, M.D.	<b>Meeting Date:</b> March 17, 2016

- C** Denotes consultants (non-voting) assisting in the review of the study when the knowledge and expertise in a particular therapeutic area is not available among the voting members
- A** Denotes members abstaining from the vote
- ✓ Denotes (voting) members who were in attendance at the meeting and reviewed the study information

	NAME	DEGREES/ CERTS.	BOARD POSITION	EXPERIENCE	AFFILIATION WITH IRB	ALTERNATE FOR
✓	<sup>M</sup> Susan Parker Ginnings, Chairman <sup>Th</sup> Susan Parker Ginnings	R.Ph.	Scientific	Retired; Hospital Pharmacy Supervisor	Non-affiliated Paid Consultant	Scientific members
	<sup>M</sup> Levi Machado, Co-chair	CCRP	Non- scientific	IRB Coordinator, administrative support for IntegReview;	Full time Employee	Non-scientific members
	<sup>M</sup> Olga Obrda	B.S. (Chemistry)	Scientific	BD Representative; previously employed as Project Management and Business Development for CRO	Non-affiliated Paid Consultant	Scientific members
	<sup>M</sup> Jennifer Christensen	Pharm. D., BCPS	Scientific	Internal Medicine, Investigational Drugs, Neuropharmacology research scientist	Non-affiliated Paid Consultant	Scientific members
	<sup>M</sup> Susan Krivacic	B.A. (German), M.P.Aff (Public Affairs)	Scientific	Consultant and patient advocate for oncology trials; previously employed as Senior Executive and Executive Director for CRO	Non-affiliated Paid Consultant	Scientific members
✓	<sup>M</sup> Matthew Pfeiffer	Ph.D.	Scientific	Project manager for CRO; Pharmacology, Toxicology, representative for first in human studies; clinical and research experience, CNS, Infectious disease, Metabolic/Endocrine Disorders, Oncology	Non-affiliated Paid Consultant	Scientific members

<sup>M</sup> Denotes regular Monday board members <sup>T</sup> Denotes regular Tuesday board members <sup>W</sup> Denotes regular Wednesday board members <sup>Th</sup> Denotes regular Thursday board members  
<sup>F</sup> Denotes regular Friday board members Other members are alternates All regular Board members can serve as alternates on other Boards as specified by their positions (e.g. Scientific for Scientific)  
 Non-scientific members represent the general perspective of study participants  
**Note: In addition to our regular members, we have access to specialists in therapeutic areas not represented on this roster.**

# INTEG<sup>i</sup> REVIEW IRB

<b>Sponsor Name:</b> American Research Corporation at Texas Liver Institute	<b>Protocol Number:</b> TLI_IIS_01_2015
<b>Principal Investigator Name:</b> Fred Poordad, M.D.	<b>Meeting Date:</b> March 17, 2016

	NAME	DEGREES/ CERTS.	BOARD POSITION	EXPERIENCE	AFFILIATION WITH IRB	ALTERNATE FOR
	<sup>T</sup> Charles F. Ryan, Chairman <sup>W</sup> Charles F. Ryan	Ph.D., M.S. (Pharmacology & Toxicology), R.Ph.	Scientific	Retired; representative for first time in human studies; Pharmacology, Toxicology, Radiation Safety, Radioisotope, Nutritional/Food supplements and Medical Foods	Non-affiliated Paid Consultant	Scientific members
	<sup>T</sup> Tonya Reed, Co-chair		Non-scientific	IRB Coordinator, administrative support for IntegReview; previously employed as a Project Assistant for CRO	IntegReview Employee	Non-scientific members
	<sup>T</sup> Sara Bartos	M.D.	Scientific	Licensed physician, Internal Medicine	Non-affiliated Paid Consultant	Scientific members
	<sup>T</sup> M. Alexander Kenaston	Ph.D., M.S. (Toxicology), R.N., CIP	Scientific	Toxicology Research Scientist, representative for first time in human studies, Pharmacology/ Toxicology, Licensed Registered Nurse; previously employed as Project Manager, CRA and CRC for CRO	Non-affiliated Paid Consultant	Scientific members
	<sup>T</sup> Christine du Castel	M.D.	Scientific	Medical Advisor; previously licensed to practice General Medicine in France	Non-affiliated Paid Consultant	Scientific members
	<sup>T</sup> Marcy Goodfleisch	B.S. , M.A. (Liberal Studies)	Non-scientific	Mediator (civil, family& workplace dispute resolution); previously employed as Management & Communication Consultant, Clinic Administrator for nationally recognized HIV Clinic and large FQHC community health center, Ethicist	Non-affiliated Paid Consultant	Non-scientific members

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	NAME	DEGREES/ CERTS.	BOARD POSITION	EXPERIENCE	AFFILIATION WITH IRB	ALTERNATE FOR
	<sup>W</sup> Carolyn Hensler, Chairman	B.S. (Physical Education)	Non- scientific	Quality Assurance and Quality Control Administrator for CRO; previously employed as a Clinical Research Monitor; and Project Manager	Non-affiliated Paid Consultant	Non-scientific members
	<sup>W</sup> Angelica Martinez	CCRP	Non- scientific	IRB Coordinator, administrative support for IntegReview	Full time Employee	Non-scientific members
	<sup>W</sup> Karen Haslund	M.D.	Scientific	Licensed physician, Pediatrics	Non-affiliated Paid Consultant	Scientific members
	<sup>W</sup> Raymond Carr	R.Ph.	Scientific	Staff Pharmacist	Non-affiliated Paid Consultant	Scientific members
	<sup>W</sup> Christopher P. Martin	Pharm.D., M.S., BCPS	Scientific	Clinical Assistant Professor, Division of Pharmacotherapy UT; Clinical Pharmacy Coordinator; Assistant Professor University of Oklahoma Health Sciences Center, College of Pharmacy	Non-affiliated Paid Consultant	Scientific members
✓	<sup>Th</sup> Frederick Kopec, Chairman	J.D., B.A. (Philosophy)	Non- scientific	Licensed, Practice of Law, Ethicist	Non-affiliated Paid Consultant	Non-scientific members
✓	<sup>Th</sup> Rosa S. Sandoval, Co- chair	B.S. (Chemistry), CCRP	Scientific	IRB Coordinator, administrative support for IntegReview; previously employed as Clinical Research Coordinator and Medical Research Assistant for University	Full time Employee	Scientific members
	<sup>Th</sup> Michael Romain	M.D.	Scientific	Licensed physician, Internal Medicine	Non-affiliated Paid Consultant	Scientific members
✓	<sup>Th</sup> Mary O'Connell		Scientific	Quality & Regulatory Affairs Manager; previously employed as Clinical Research Recruiter, Data Associate, Coordinator and QC Auditor for CRO, IRB Administrator, Emergency Medical Technician Paramedic	Non-affiliated Paid Consultant	Scientific members

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<sup>Th</sup> Dario Kuzmanovic	B.A., MHSc, CRA	Scientific	Research Ethics Manager; serves as a member on HIV Research Ethics Board, Research Ethics Policy & Advisory Committee, U of T REB Chairs Committee and the Research Ethics & Research Education Committee, Ethicist	Non-affiliated Paid Consultant	Scientific members
<sup>F</sup> Mary Ruwart, Chairman	Ph.D. (Biophysics); B.S. (Biochemistry)	Scientific	Research Scientist, Drug Delivery Systems, Diabetes, GI Diseases, Drug Metabolism	Non-affiliated Paid Consultant	Scientific members
<sup>F</sup> Jami Brackeen, Co-chair	CST, CCRP	Scientific	IRB Coordinator; former Quality Control Associate for IRB Regulatory Compliance; Certified Surgical Technologist	Full time Employee	Scientific members
<sup>F</sup> Laurajo Ryan	Pharm.D., MSc (Clinical Investigations), BCPS, CDE	Scientific	Clinical Assistant Professor of Pharmacy, Division of Pharmacotherapy UT, Department of Medicine UTHSCSA, Clinical Pharmacy Specialist STX VA	Non-affiliated Paid Consultant	Scientific members
<sup>F</sup> Dennis Brannon	R.Ph., B.S. (Animal Science)	Scientific	Clinical Research Consultant, Director of Pharmacy; Executive Director Clinical Development; previously employed as Senior Project Manager and CRA for CRO	Non-affiliated Paid Consultant	Scientific members
<sup>F</sup> Ashley Hutson		Non-scientific	Unemployed; previously volunteered as research subject in clinical trials	Non-affiliated Paid Consultant	Non-scientific members
<sup>F</sup> Eduardo E. Sandoval	M.D., MBA (Healthcare Administration)	Scientific	Clinical Research Consultant; previously employed as Medical Affairs/Medical Officer, Regional Senior Clinical Research Associate, Quality Assurance Auditor, Clinical Research Manager	Non-affiliated Paid Consultant	Scientific members

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	Victoria Govea	CCRP	Non-scientific	Management support for IntegReview; former IRB Coordinator, Co-chair for IntegReview	Full time Employee	Non-scientific members
	Lynn Goldman	B.S. (Nutrition), MSHP (Healthcare Administration), RD, LD, CCRP	Scientific	Management support for IntegReview; former IRB Coordinator, administrative support for IntegReview; previously employed as Research Coordinator, Health Care Administration and Education, Clinical Nutrition, Registered Dietician/Certified Pediatric Nutrition Specialist	Full time Employee	Scientific members
	Kimberly S. Cowley	Ed.D., E.S., M.A., B.A.	Non-scientific	Educational researcher/evaluator; Managing Evaluator; previously employed as Director of Research, Evaluation & Expertise, Executive Director, served as IRB member and Chair	Non-affiliated Paid Consultant	Non-scientific
✓	Christina H. Walker	M.D., B.S.	Scientific	Licensed physician	Non-affiliated Paid Consultant	Scientific

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