STATISTICAL ANALYSIS PLAN

Study Title:	A Phase 3, Multicenter, Open-Label Study to Investigate the Efficacy and Safety of Sofosbuvir/Velpatasvir Fixed Dose Combination for 12 Weeks in Subjects with Chronic HCV
Name of Test Drug:	Sofosbuvir/Velpatasvir Fixed-Dose Combination
Study Number:	GS-US-342-1518
Protocol Version (Date):	Amendment 1: 21 April 2015
Analysis Type:	SVR12 and Final Analysis
Analysis Plan Version:	1.0
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Analysis Plan Author:	PPD

CONFIDENTIAL AND PROPRIETARY INFORMATION

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LIST OF ABBREVIATIONS

AE	adverse event
ALT	alanine aminotransferase
ANC	absolute neutrophil count
APRI	AST:platelet ratio index
APTT	activated partial thromboplastin time
AST	aspartate transaminase
ATC	anatomical therapeutic chemical
BLQ	below the limit of quantitation
BMI	body mass index
BPM	beats per minute
CI	confidence interval
CMH	Cochran-Mantel-Haenszel
CSR	clinical study report
DAA	direct acting antiviral
DMC	data monitoring committee
ECG	electrocardiogram
eCRF	electronic case report form
eGFR	estimated glomerular filtration rate
EOT	end of treatment
FAS	full analysis set
FDC	fixed dose combination
FU	follow-up
GT	genotype (viral)
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
HLGT	high level group term
HLT	high level term
ID	identification
IL28B	IL28B genotype
INR	International Normalized Ratio of prothrombin time
IWRS	Interactive Web Response System
LLOQ	lower limit of quantitation
LLT	lower level term
MCV	mean corpuscular volume or mean cell volume
MedDRA	Medical Dictionary for Regulatory Activities
Peg-IFN	pegylated interferon
PT	preferred term
RBC	red blood cell count

Q1	first quartile
Q3	third quartile
RBC	red blood cell
RBV	ribavirin
RNA	ribonucleic acid
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation
SE	standard error
SOC	system organ class
SOF	sofosbuvir (Sovaldi®)
SVR	sustained virologic response
SVRx	sustained virologic response x weeks after stopping study drug
TE	treatment-emergent
TFLs	tables, figures, and listings
TND	target not detected
ULN	upper limit of the normal range
VEL	velpatasvir (GS-5816)
WBC	white blood cell
WHO	World Health Organization

1. INTRODUCTION

This statistical analysis plan (SAP) describes the statistical analysis methods and data presentations to be used in tables, figures, and listings (TFLs) in the clinical study report (CSR) for Study GS-US-342-1518. This SAP is based on the study protocol amendment 1 dated 21 April 2015 and the electronic case report form (eCRF). The SAP will be finalized before database finalization. Any changes made after the finalization of the SAP will be documented in the CSR.

1.1. Study Objectives

The primary objectives of this study are as follows:

- To evaluate the efficacy of treatment with sofosbuvir (SOF)/velpatasvir (VEL, GS-5816) fixed dose combination (FDC) for 12 weeks in subjects with chronic HCV infection as measured by the proportion of subjects with sustained viral response 12 weeks after cessation of treatment (SVR12)
- To evaluate the safety and tolerability of treatment with SOF/VEL for 12 weeks

The secondary objectives of this study are:

- To determine the proportion of subjects with SVR at 4 and 24 weeks after cessation of treatment (SVR4 and SVR24)
- To evaluate the proportion of subjects with virologic failure
- To evaluate the kinetics of circulating HCV RNA during treatment and after cessation of treatment
- To evaluate the emergence of viral resistance to SOF and VEL during treatment and after cessation of treatment

The exploratory objectives of this study are:

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1.2. Study Design

This is an international, multicenter, open-label study that will evaluate the safety, tolerability and antiviral efficacy of SOF/VEL for 12 weeks in treatment-naïve and treatment-experienced adults with chronic HCV infection. Subjects with or without cirrhosis will be enrolled.

Approximately 20% of subjects may be treatment experienced and approximately 20% of subjects may have compensated cirrhosis at screening.

Subjects with chronic HCV infection will be enrolled to receive SOF/VEL once daily for 12 weeks.

This multi-regional clinical trial (MRCT) is planned to be conducted in China, Malaysia, Singapore, Thailand, and Vietnam. China will be considered Region 1. Malaysia, Singapore, Thailand, and Vietnam, which are all located in Southeast Asia, will be considered Region 2.

Approximately 360 subjects will be enrolled in the study in total. The approximate number of subjects to be enrolled in each region according to HCV genotype is represented in the table below:

HCV GT (Prior Rx History)	**GT-1 (TN, TE)**	**GT-2 (TN, TE)**	**GT-3 (TN, TE)**	**GT-4,5,6 (TN, TE)**	**Total**
Region 1 (China)	80	60	60	60	260
Region 2 (Malaysia, Singapore, Thailand, Vietnam)	100				100

Rx = Treatment
TN = Treatment Naïve, TE = Treatment Experienced

It is expected that a small number of subjects whose HCV genotype cannot be determined by the central laboratory (HCV genotype indeterminate) may also be enrolled.

The schedule of assessments is provided as an appendix to the SAP (Appendix 1).

The total time to complete all study visits is up to approximately 42 weeks including the following periods:

- 42-day (6-week) screening period
- 12-week treatment period
- Up to 24-week posttreatment period

1.3. Sample Size and Power

The sample size justification is based on the Region 1 population. A sample size of 260 subjects in Region 1 will provide more than 80% power to detect an improvement of at least 6 percentage points in SVR12 rate from the performance goal of 85% by using a two-sided exact one-sample binomial test at the significance level of 0.05.

In addition, a confidence interval approach will be used to estimate the SVR12 rates for Region 2 and for the overall population (ie, combined Region 1 and Region 2). With 100 subjects from Region 2, and 360 subjects from the overall population, the 2-sided 95% exact CIs for different observed SVR12 rates are presented in the table below.

Region	Observed SVR12 rate	2-sided 95% exact CI
Region 2 (n=100)	80% (80 out of 100)	71% - 87%
	90% (90 out of 100)	82% - 95%
Overall (n=360)	80% (288 out of 360)	75% - 84%
	90% (324 out of 360)	86% - 93%

2. TYPE OF PLANNED ANALYSIS

2.1. Data Monitoring Committee

This study does not have a data monitoring committee (DMC).

2.2. Interim Analysis

2.2.1. Posttreatment Week 4 Analysis

A Posttreatment Week 4 analysis will be conducted for administrative purposes after all subjects complete the Posttreatment Week 4 visit or prematurely discontinue from the study. All safety and efficacy data through the Posttreatment Week 4 visit will be included (SVR12 will not be evaluated at this time). The results will be restricted to a limited group of individuals within Gilead Sciences, Inc. (Gilead). There will be no changes to the study design, study conduct, or the sample size as a result of this administrative analysis.

2.2.2. Primary Efficacy Endpoint Analysis

The analyses for the primary endpoint SVR12 will be conducted for Region 1, Region 2, and Overall after all subjects complete the posttreatment Week 12 visit or prematurely discontinue from study. All the safety and efficacy data through the posttreatment Week 12 visit will be cleaned, finalized and included for the analysis.

2.3. Final Analysis

After all subjects have completed the study, outstanding data queries have been resolved, and the database has been cleaned and finalized, the final analysis of the data will be performed.

3. GENERAL CONSIDERATIONS FOR DATA ANALYSES

Analysis results will be presented using descriptive statistics. For categorical variables, the number and percentage of subjects in each category will be presented; for continuous variables, the number of subjects [n], mean, standard deviation [SD] or standard error [SE], median, first quartile [Q1], third quartile [Q3], minimum, and maximum will be presented.

Statistical tests will be two-sided and performed at the 5% significance level unless otherwise prespecified in Section 6.1.

Data collected in the study will be presented in by-subject listings for all subjects in the Safety Analysis Set, unless otherwise specified. All by-subject listings will be presented by region and subject identification (ID) number in ascending order, unless otherwise specified.

3.1. Analysis Sets

Analysis sets define the subjects to be included in an analysis. Analysis sets and their definitions are provided in this section. The number of subjects eligible for each analysis set will be provided. Subjects who were excluded from each analysis set will be summarized or provided in a by-subject listing with reasons for exclusion by region.

3.1.1. All Enrolled Analysis Set

The All Enrolled Analysis Set includes all subjects who were enrolled in the study. Subjects are grouped within the All Enrolled Analysis Set by genotype (GT) and region.

3.1.2. Full Analysis Set

The Full Analysis Set (FAS) includes all subjects who were enrolled into the study and received at least 1 dose of study drug. The study drug in this study is SOF/VEL. Subjects are grouped within the FAS by region and genotype.

This is the primary analysis set for efficacy analyses.

3.1.3. Safety Analysis Set

The Safety Analysis Set includes all subjects who were enrolled into the study and received at least 1 dose of study drug. Subjects are grouped by region.

This is the primary analysis set for safety analyses.

3.2. Subject Grouping

For analyses based on All Enrolled Analysis Set and Full Analysis Set, subjects will be grouped by region for primary analysis of the primary endpoint and grouped by region and genotype for all other analyses. Unless otherwise specified, groups by genotype include GT1a, GT1b, GT1 (Total), GT2, GT3, GT4, GT5, GT6, Indeterminate, and Total, and groups by region include Region 1, Region 2, and Overall. For analyses based on the Safety Analysis Set, subjects will be grouped by region and genotype for demographic information and grouped by region for all other safety analyses.

3.3. Examination of Subject Subsets

Subject subsets will be explored for the primary efficacy endpoint, SVR12. The subject subsets include the following:

- age (< 65 years, ≥ 65 years)
- sex (male, female)
- baseline body mass index (BMI) (< 25 kg/m^2 , ≥ 25 kg/m^2)
- baseline HCV RNA (< 800,000 IU/mL, ≥ 800,000 IU/mL; < 5 $\log_{10}$ IU/mL, ≥ 5 $\log_{10}$ IU/mL)
- baseline ALT (≤ 1.5 × upper limit of normal [ULN], > 1.5 × ULN)
- IL28B (CC, non-CC; with non-CC further broken down to CT, TT)
- cirrhosis (presence, absence, missing)
- prior HCV treatment experience (treatment naïve, treatment experienced)
- prior HCV treatment (DAA+PEG+RBV, INTERFERON+RBV, PEG+RBV, Other) for treatment-experienced subjects
- most recent HCV treatment response (non-responder, relapse/breakthrough, early treatment discontinuation, met a virologic stopping rule, not otherwise listed, unknown) for treatment-experienced subjects
- adherence to study regimen (<80%, ≥ 80%)

3.4. Missing Data and Outliers

3.4.1. Missing Data

In general, missing data will not be imputed unless methods for handling missing data are specified.

For missing last dosing date of study drug, imputation rules are described in Section 3.7.1. The handling of missing or incomplete dates for adverse event (AE) onset is described in Section 7.2.5.2, and for prior and concomitant medications in Section 7.5.

For analyses of categorical HCV RNA data, missing posttreatment HCV RNA data will have the missing data imputed. Missing on-treatment HCV RNA will have the missing data imputed up to the time of the last dose (for on-treatment displays). If the study day associated with the last dosing date is greater than or equal to the lower bound of a visit window, and the value at the visit is missing, the value will be imputed. If the study day associated with the last dosing date is less than the lower bound of a visit window then the on-treatment value at that visit will remain missing.

If a HCV RNA data point is missing and is preceded and followed in time by values that are "< LLOQ target not detected (TND)", then the missing data point will be set to "< LLOQ TND". If a data point is missing and preceded and followed by values that are "< LLOQ detected", or preceded by "< LLOQ detected" and followed by "< LLOQ TND", or preceded by "< LLOQ TND" and followed by "< LLOQ detected", then the missing value will be set to "< LLOQ detected". In these situations the data point will be termed a bracketed success; otherwise, the data point will be termed a bracketed failure (ie, ≥ LLOQ detected). If a data point is missing and is not bracketed, the missing data point will also be termed a failure (ie, ≥ LLOQ detected) except for SVR24, which will be imputed according to SVR12 status. Success for SVR12 who have no further HCV RNA measurements collected will be counted as a success for SVR24 due to the high correlation between these 2 endpoints.

For the analyses of continuous HCV RNA efficacy data, when and only when a missing HCV RNA value is imputed as < LLOQ TND or < LLOQ detected according to the imputation rule described above, the corresponding continuous value will be imputed to LLOQ – 1 IU/mL. No other imputation will be performed for continuous HCV RNA data.

For health-related quality of life data SF-36, missing data will not be imputed.

3.4.2. Outliers

Outliers will be identified during the data management and data analysis process, but no sensitivity analyses will be conducted. All data will be included in the data analysis.

3.5. Multiple Comparisons

No multiplicity adjustment will be made.

3.6. Data Handling Conventions and Transformations

By-subject listings will be presented for all subjects in the Safety Analysis Set and sorted by region, subject ID number, visit date, and time (if applicable) unless otherwise specified. Data collected on log forms, such as AEs, will be presented in chronological order within subject.

Age (in years) on the date of the first dose of study drug and sex at birth will be used for analyses and presentation in listings.

If a subject was not dosed with study drug at all, then the date the informed consent was signed will be used instead of the first dose date of study drug. For some countries, only birth year is collected on the CRF. In those cases, "01 January" will be used for the unknown birth day and month for the purpose of age calculation, unless age is captured on the CRF.

Non-PK data that are continuous in nature but are less than the lower limit of quantitation or above the upper limit of quantitation will be imputed as follows:

- A value that is one unit less than the limit of quantitation will be used for calculation of descriptive statistics if the datum is reported in the form of "< x" (where x is considered the limit of quantitation). For example, if the values are reported as < 50 and < 5.0, values of 49 and 4.9, respectively, will be used for calculation of summary statistics. An exception for this rule is any value reported < 1. For the values reported as < 1 or < 0.1, value of 0.9 or 0.09 will be used for calculation of summary statistics.

- A value that is one unit above the limit of quantitation will be used for calculation of descriptive statistics if the datum is reported in the form of "> x" (where x is considered the limit of quantitation). Values with decimal points will follow the same logic as above.

- The limit of quantitation will be used for calculation of descriptive statistics if the datum is reported in the form of "≤ x" or "≥ x" (where x is considered the limit of quantitation).

The COBAS® TaqMan® HCV Quantitative Test, v2.0 was used to determine HCV RNA results in this study. The lower limit of quantitation (LLOQ) of the assay is 15 IU/mL.

When the calculated HCV RNA value is within the linear range of the assay, then the result will be reported as the "<< numeric value>> IU/mL". This result will be referred to in this document as the numeric result or as "≥ LLOQ detected" for categorical result.

When HCV RNA is not detected, the result is reported as "No HCV RNA detected" or "target not detected". This result will be referred to in this document as "< LLOQ target not detected" or "< LLOQ TND".

When the HCV RNA IU/mL is less than LLOQ of the assay, the result is reported as "< 15 IU/mL HCV RNA detected". This result will be referred to in this document as "< LLOQ detected".

The overall category of HCV RNA < LLOQ includes "< LLOQ TND" and "< LLOQ detected."

For numerical HCV RNA data, values below LLOQ will be set to the LLOQ – 1 IU/mL (ie, 14 HCV RNA IU/mL). HCV RNA values returned as "No HCV RNA detected" will also be set to 14 IU/mL.

For selected analyses, HCV RNA data (IU/mL) will be transformed to the logarithmic (base 10) scale ($\log_{10}$ IU/mL).

3.7. Visit Windows

3.7.1. Definition of Study Day

Study day is the day relative to the date of the first dose of study drug. Study Day 1 will be defined as the day of first dose of study drug administration.

Study day will be calculated from the date of first dose of study drug administration and derived as follows:

- For postdose study days: Assessment Date – First Dose Date + 1

- For days prior to the first dose: Assessment Date – First Dose Date

The last dose date will be the end date on study drug administration eCRF for the record where the "subject permanently discontinued" flag is 'Yes'.

If there are subjects for whom the date of last study drug is unknown due to the reason that the subject was lost to follow-up and not able to be contacted, the date of last dose will be estimated using the maximum of nonmissing study drug start or stop dates, visit dates and laboratory collection dates (posttreatment visits and unscheduled visits are not included).

3.7.2. Analysis Windows

Subject visits might not occur on protocol-specified days. Therefore, for the purpose of analysis, observations will be assigned to analysis windows.

In general, the baseline value will be the last nonmissing value on or prior to the first dose date of study drug.

HCV RNA, vital signs, and safety laboratory data collected up to the last dose date + 3 days are considered to be on-treatment data and HCV RNA, vital signs and safety laboratory data collected after the last dose date + 3 days are considered posttreatment data. The analysis windows for on-treatment HCV RNA, vital signs and safety laboratory data are provided in Table 3-1.

Table 3-1. Analysis Windows for On-treatment HCV RNA, Vital Signs and Safety Laboratory Data

Nominal Visit	Nominal Day	Lower Limit	Upper Limit
Baseline	1	(none)	1
Week 1	7	2	11
Week 2	14	12	21
Week 4	28	22	35
Week 6	42	36	49
Week 8	56	50	63
Week 10	70	64	77
Week 12	84	78	≥ 85

HCV RNA, vital sign, and safety laboratory data collected after the last dose date + 3 days will be assigned to the posttreatment follow-up (FU) visits. Visit windows will be calculated from the last dose date (ie, FU Day = collection date minus the last dose date) as shown in Table 3-2.

Table 3-2. Analysis Windows for Posttreatment HCV RNA, Vital Signs and Safety Laboratory Data

Nominal FU [a] Visit	HCV RNA			Vital Signs and Safety Laboratory Data [b]		
	Nominal FU Day	Lower Limit	Upper Limit	Nominal FU Day	Lower Limit	Upper Limit
FU-4	28	21	69	28	4	30
FU-12	84	70	146	NA	NA	NA
FU-24	168	147	210	NA	NA	NA

a FU-x visit = posttreatment Week-x follow-up visit.
b Vital signs and safety labs will only be summarized for the FU-4 visit (up to 30 days after last dose).

ECG data collected up to the last dose date + 3 days are considered to be on-treatment data. Qualitative assessments of whether the ECG is normal or abnormal will be assessed for on-treatment data based on the visit windows as shown in Table 3-3.

Table 3-3. Analysis Windows for On-treatment ECG Data

Nominal Visit	Nominal Day	Lower Limit	Upper Limit
Baseline	1	(none)	1
Week 1	7	2	45
Week 12	84	46	(none)

Note: ECGs are to be collected at screening, Day 1, Week 1, and Week 12 or End of Treatment. For purposes of analysis, baseline value will be the last available value prior to the first dose of study drug and end of treatment value will be the last available value on or prior to the last dose date + 3 days.

3.7.3. Selection of Data in the Event of Multiple Records in an Analysis Window

Depending on the statistical analysis method, single values may be required for each analysis window. For example, change from baseline by visit usually requires a single value, whereas a time-to-event analysis would not require 1 value per analysis window.

If multiple valid nonmissing numeric observations exist in an analysis window, records will be chosen based on the following rules if a single value is needed:

- For baseline, the last available record on or prior to the date of the first dose of study drug will be selected. If there are multiple records with the same time or no time recorded on the same day, average (arithmetic mean) will be used for the baseline value. If multiple ECG measurements occur on the same day prior to first dose of any study drug, the average will be used considered as baseline value for continuous data, regardless of the timing of these multiple ECG measurements.

- For postbaseline visits:
  - The record closest to the nominal day for that visit will be selected except for HCV RNA posttreatment follow-up visits, for which the latest record in the analysis window will be selected.
  - If there are 2 records that are equidistant from the nominal day, the later record will be selected.
  - If there is more than 1 record on the selected day, the average will be taken, unless otherwise specified.

If multiple valid nonmissing categorical observations exist in a window, records will be selected as follows:

- For baseline, the last available record on or prior to the date of the first dose of study drug will be selected. If there are multiple records with the same time or no time recorded on the same day, the value with the lowest severity will be selected (eg, normal will be selected over abnormal). If multiple ECG measurements occur on the same day prior to the first dose of any study drug, the value with the lowest severity will be selected regardless of the timing of these multiple ECG measurements.
- For postbaseline visits, follow the same rules described above for postbaseline numeric observations, except that if there are multiple records on the same day, the most conservative value will be selected (eg, abnormal will be selected over normal).

4. SUBJECT DISPOSITION

4.1. Subject Enrollment and Disposition

A summary of subject enrollment will be provided for each investigator. The summary will present the number and percentage of subjects in the Safety Analysis Set. The denominator for the percentage calculation will be the total number of subjects analyzed.

A summary of subject disposition will be provided by region and genotype. This summary will present the number of subjects screened, the number of subjects enrolled, the number of subjects enrolled but never treated, and the number and percentage of subjects in each of the categories listed below. For the "Treated" category, the denominator for the percentage calculation will be the total number of subjects enrolled for each column. For all other categories, the denominator for the percentage calculation will be the total number of subjects in the Safety Analysis Set for each column.

- Treated (Safety Analysis Set)
- In FAS
- Continuing study treatment if applicable
- Completed study treatment
- Did not complete study treatment with reasons for premature discontinuation of study treatment
- Completed study
- Did not complete the study with reasons for premature discontinuation of study

Among subjects who completed study treatment and who discontinued study treatment, the number and percentage of subjects will be summarized for:

- Who had no HCV posttreatment Week 4 assessment and thereafter (No HCV FU-4 and thereafter)
- Who had HCV posttreatment Week 4 assessment but no HCV posttreatment Week 12 assessment and thereafter (With HCV FU-4 but No FU-12 and thereafter)

If a subject did not have any HCV RNA assessment ≥ 21 days after the last dose of any study drug (ie, lower bound of FU-4 visit for HCV RNA data), the subject is categorized as having "No HCV FU-4 and thereafter". If a subject had the HCV FU-4 assessment but did not have any HCV RNA assessment ≥ 70 days after the last dose of any study drug (ie, lower bound of FU-12 visit for HCV RNA data), the subject is categorized as having "With HCV FU-4 but No FU-12 and thereafter".

In addition, the total number of subjects who were enrolled, and the number of subjects in each of the disposition categories listed above will be depicted by a flowchart.

The following by-subject listings will be provided by region and subject ID number in ascending order to support the above summary tables:

- Disposition for subjects who complete study treatment and study
- Disposition for subjects who did not complete study treatment and/or study with reasons for premature discontinuation of study treatment and/or study
- Lot number and kit ID (if applicable)

4.2. Extent of Exposure

Extent of exposure to study drug will be examined by assessing the total duration of study drug exposure and the level of adherence to the study drug regimen specified in the protocol.

4.2.1. Duration of Exposure to Study Drug

Total duration of exposure to study drug will be defined as last dose date minus first dose date plus 1, regardless of any temporary interruptions in study drug administration, and will be expressed in weeks using up to 1 decimal place (eg, 4.8 weeks).

The total duration of exposure to study drug will be summarized using descriptive statistics (n, mean, SD, median, Q1, Q3, minimum, and maximum) and using the number (ie, cumulative counts) and percentage of subjects exposed through the following time periods: baseline (Day 1), Week1 (Day 7), Week 2 (Day 14), Week 4 (Day 28), Week 6 (Day 42), Week 8 (Day 56), Week 10 (Day 70), and Week 12 (Day 84). A 3-day window is applied to the last planned on-treatment visit to match with the protocol-specified visit window, ie, number of subjects exposed through week 12 is calculated as the number of subjects who were exposed to study drug for at least 81 days. Summaries will be provided by region for the Safety Analysis Set.

4.2.2. Adherence to Study Drug

The presumed total number of tablets administered to a subject will be determined by the data collected on the drug accountability CRF using the following formula:

$$\text{Total Number of Doses Administered} = \left(\sum \text{No. of Tablets Dispensed}\right) - \left(\sum \text{No. of Tablets Returned}\right)$$

The level of adherence to the study drug regimen will be assessed based on the total amount of study drug administered relative to the total amount of study drug prescribed at baseline.

The level of adherence will be expressed in percentage using the following formula:

$$\text{Level of Adherence (\%)} = \left(\frac{\text{Total Amount of Study Drug Administered}}{\text{Total Amount of Study Drug Prescribed at baseline}} \right) \times 100$$

Note: If calculated adherence is greater than 100%, the result will be set to 100%.

In this study, the total amount of SOF/VEL (400 mg/100 mg) prescribed for 12 weeks would require 84 tablets.

Subjects who prematurely discontinue study drug for lack of efficacy (ie, virologic failure) will have the total amount of study drug prescribed calculated up to the first date when virologic failure criteria were met. For virologic failure confirmed by 2 consecutive measurements the date of the first measurement will be used. If there are study drug bottles dispensed on or after the subject first met virologic failure criteria, these bottles will not be included in the calculation of adherence. If a bottle is dispensed and the bottle is returned empty, then the number of tablets returned will be entered as zero. If a bottle is dispensed but not returned (missing), the number of tablets taken from that bottle will be counted as zero.

Descriptive statistics for the level of adherence (n, mean, SD, median, Q1, Q3, minimum, and maximum) with the number and percentage of subjects belonging to adherence categories (eg, $< 80\%$, ≥ 80 to $< 90\%$, $\geq 90\%$) will be provided by region and genotype for the Safety Analysis Set.

No inferential statistics will be provided for duration of exposure and adherence to study drug.

A separate by-subject listing of study drug administration and drug accountability will be provided by region, subject ID number (in ascending order) and visit (in chronological order).

4.3. Protocol Deviations

A summary of important protocol deviations will be provided by the Clinical Operations group for subjects in the Safety Analysis Set.

A by region, by-subject listing will be provided for those subjects who violate at least 1 inclusion or exclusion criterion. The listing will present the entry criterion (or criteria if more than 1 violation) that subjects did not meet and related comments, if collected.

5. BASELINE CHARACTERISTICS

5.1. Demographics

Subject demographic variables (ie, age, sex, race, and ethnicity) will be summarized by region and genotype using descriptive statistics (n, mean, SD, median, Q1, Q3, minimum, and maximum) for age, and using the numbers and percentages of subjects for age categories (< 65 years, ≥ 65 years), sex, race, and ethnicity. Age is calculated in years at the date of initial study drug administration. If a subject did not receive study drug after enrollment, the subject's age will be calculated from the date that the subject signed the informed consent form. The summary of demographic data will be provided for the Safety Analysis Set.

A by-subject demographic listing, which includes the date the informed consent was signed, will be provided by region and subject ID number in ascending order.

5.2. Baseline Characteristics

Baseline characteristics include:

- body mass index (BMI; in kg/m^2) as a continuous variable and as categories (< 25 kg/m^2, ≥ 25 kg/m^2)
- HCV genotype and subtype
- IL28B (CC, CC, non-CC; with non-CC further broken down to CT, TT)
- baseline HCV RNA (log10 IU/mL) as a continuous variable and as categories (< 800,000 IU/mL, ≥ 800,000 IU/mL; < 5 $\log_{10}$ IU/mL, ≥ 5 $\log_{10}$ IU/mL)
- baseline ALT (U/L) as a continuous variable and as categories (≤1.5 x ULN, > 1.5 x ULN)
- cirrhosis (presence, absence, missing)
- cirrhosis determination method (Liver Biopsy, Fibrotest/APRI, Transient Elastography, Fibrotest/APRI and Transient Elastography, and Not determined per protocol)
- prior HCV treatment experience (treatment naïve, treatment experienced)
- prior HCV treatment (DAA+PEG+RBV, INTERFERON+RBV, PEG+RBV, Other) for treatment-experienced subjects
- most recent HCV treatment response (non-responder, relapse/breakthrough, early treatment discontinuation, met a virologic stopping rule, not otherwise listed, unknown) for treatment-experienced subjects
- estimated glomerular filtration rate (eGFR) using the Cockcroft-Gault equation

eGFR will be calculated by the Cockcroft-Gault method: $eGFR_{CG}$ (mL/min) = [(140 – age (yrs)) × weight (kg) × (0.85 if female)] / (serum creatinine (mg/dL) × 72), where weight is total body mass in kilograms.

These baseline characteristics will be summarized by region and genotype using descriptive statistics (n, mean, SD, median, Q1, Q3, minimum, and maximum) for continuous variables and using the numbers and percentages of subjects for categorical variables. The summary of baseline characteristics will be provided for the Safety Analysis Set.

A by-subject listing of baseline characteristics will be provided by region and subject ID number in ascending order.

A separate by-subject data listing for cirrhosis determination will be provided for all subjects at screening.

A separate by-subject data listing for prior HCV treatment and response will be provided for all treatment-experienced subjects. The listing will display the prior HCV regimen(s) and treatment(s) including the treatment duration, and the prior HCV treatment response.

5.3. Medical History

A by-subject listing of disease-specific medical history will be provided by region and subject ID number (in ascending order) and medical history of abnormalities (in chronological order).

6. EFFICACY ANALYSES

6.1. Primary Efficacy Endpoint

6.1.1. Definition of the Primary Efficacy Endpoint

The primary efficacy endpoint is SVR12 defined as HCV RNA < LLOQ 12 weeks after discontinuation of all study drugs in the FAS. The COBAS® TaqMan® HCV Quantitative Test, v2.0 for use with Ampliprep will be used to measure HCV RNA.

6.1.2. Statistical Hypothesis for the Primary Efficacy Endpoint

In the primary efficacy analysis, the SVR12 rate in Region 1 will be compared to the pre-specified performance goal of 85% by using a two-sided exact one-sample binomial test at the 0.05 significance level. The null (H0) and alternative (H1) hypotheses used to assess superiority of SOF/VEL in Region 1 relative to the performance goal of 85% are:

- H0: SVR12 rate = 85%
- H1: SVR12 rate ≠ 85%

It is difficult to characterize a single historical control rate for all genotypes included in this study given the different standards of care of each genotype (some of which include interferon), and the lack of historical data for genotype 4, 5, and 6 participants. Given these difficulties, rather than use a historical control rate as the basis for assessing the primary endpoint, a pre-specified performance goal is defined as a benchmark against which the efficacy of SOF/VEL will be tested. The benchmark sets a high bar of 85%. The basis for this benchmark includes the overall trend toward increasing SVR rates in recent years, the higher SVR rates observed with Peg-IFN + RBV treatment in Chinese and other Asian subjects {Yu 2009} compared with other races, and the general appeal of using a fixed clinically relevant threshold as a measure of treatment benefit {Weins 2013} of SOF/VEL.

6.1.3. Primary Analysis of the Primary Efficacy Endpoint

The 2-sided 1-sample exact binomial test will be used to test the statistical hypotheses described above. The 2-sided 95% exact confidence interval (CI) based on the Clopper-Pearson method {Clopper 1934} will be provided for the SVR12 rate for Region 1.

The point-estimate with the 2-sided 95% exact confidence interval (CI) using the binomial distribution (Clopper-Pearson method) will also be constructed for the SVR12 rates for Region 2 and for the overall population.

6.1.4. Subgroup Analysis of the Primary Efficacy Endpoint

Point estimates and 95% exact confidence intervals (CIs) of the SVR12 rates by region and genotype will be displayed for each subgroup outlined in Section 3.3.

A Forest plot will graphically present estimates and 95% CIs on the SVR12 rates for each of the subgroups.

6.2. Secondary Efficacy Endpoints

6.2.1. Definition of Secondary Efficacy Endpoints

Secondary efficacy endpoints include the following:

- The percentage of subjects with HCV RNA < LLOQ 4 and 24 weeks after discontinuation of treatment (SVR 4 and SVR 24)
- The percentage of subjects with HCV RNA < LLOQ while on treatment by study visit
- HCV RNA (log_{10} IU/mL) and change from baseline in HCV RNA (log_{10} IU/mL) through end of treatment (EOT)
- The percentage of subjects with virologic failure as the following:

  On-treatment virologic failure

  — HCV RNA ≥ LLOQ after having previously had HCV RNA < LLOQ, while on treatment, confirmed with 2 consecutive values (note, second confirmation value can be posttreatment), or last available on-treatment measurement with no subsequent follow-up values (ie, breakthrough)

  — 1 log_{10}IU/mL increase in HCV RNA from nadir while on treatment, confirmed with 2 consecutive values (note, second confirmation value can be posttreatment), or last available on-treatment measurement with no subsequent follow-up values (ie, rebound)

  — HCV RNA persistently ≥ LLOQ through 8 weeks of treatment (ie, nonresponse)

  Relapse

  — HCV RNA ≥ LLOQ during the posttreatment period having achieved HCV RNA < LLOQ at end of treatment, confirmed with 2 consecutive values or last available posttreatment measurement

- Characterization of HCV drug resistance substitutions at baseline, during, and after therapy with SOF/VEL

6.2.2. Analysis Methods for Secondary Efficacy Endpoints

For analyses of HCV RNA < LLOQ by visit while on treatment and during the posttreatment (SVR) follow-up period, subjects will be assigned a value at each visit based on the analysis visit windows specified in Section 3.7.2. Missing values will be imputed based on the categorical imputation rules described in Section 3.4.1. The two-sided 95% exact confidence interval based on Clopper-Pearson method will be provided for the percentage of subjects with HCV RNA < LLOQ at each visit by region and genotype. The overall category for "HCV RNA < LLOQ" will be split into the following 2 subcategories: "< LLOQ TND" for subjects with target not detected and "< LLOQ detected" for subjects with < LLOQ detected in tabular displays.

Graphs for the percentage of subjects with HCV RNA < LLOQ over time during treatment will be displayed.

Summary statistics will be presented for absolute values and change from baseline in HCV RNA (log_{10} IU/mL) by visit through EOT. Imputation rules described in Section 3.4.1 will be used to assign HCV RNA values for missing values at a visit that are bracketed by "< LLOQ TND" and/or "< LLOQ detected". Otherwise, a missing = excluded analysis will be performed. Plots of the mean ± SD and median (Q1, Q3) of absolute values and changes from baseline in HCV RNA through EOT will be presented.

For the SVR12 endpoint analysis, a summary table of the number and percentage of subjects with SVR12, virologic failure (VF), and Other by region and genotype will be created. All subjects who achieve SVR12 will be categorized as SVR12. Virologic failure will be descriptively summarized as "on-treatment virologic failure" and relapse (which will be broken down by study drug completed yes/no). Subjects who do not achieve SVR12 and do not meet criteria for VF will be categorized as "Other". The denominator for relapse will be the number of subjects who had HCV RNA < LLOQ on their last observed on-treatment HCV RNA measurement; otherwise, the denominator will be the number of subjects in the FAS.

A concordance table between SVR12 and SVR24 will be provided by region and genotype. Subjects with both observed SVR12 and observed SVR24 data will be included for this analysis.

Drug resistant substitutions will be analyzed and presented as part of the Clinical Study Report.

6.3. Exploratory Efficacy Endpoints

6.3.1. Definition of Exploratory Efficacy Endpoints

PPD

PPD

6.3.2. Analysis Methods for Exploratory Efficacy Endpoints

PPD

6.4. Changes From Protocol-Specified Efficacy Analyses

There are no planned changes from protocol-specified efficacy analyses.

7. SAFETY ANALYSES

7.1. Safety Endpoints

The primary safety endpoint is any AE leading to permanent discontinuation of study drug(s).

7.2. Adverse Events and Deaths

7.2.1. Adverse Event Dictionary

Clinical and laboratory adverse events (AEs) will be coded using the current version of MedDRA. System organ class (SOC), high-level group term (HLGT), high-level term (HLT), preferred term (PT), and lower-level term (LLT) will be provided in the AE dataset.

7.2.2. Adverse Event Severity

Adverse events are graded by the investigator as Grade 1, 2, 3, or 4 according to toxicity criteria specified in the protocol. The severity grade of events for which the investigator did not record severity will be categorized as "missing" for tabular summaries and data listings and the most severe will be considered (for sorting purpose only) in data presentation.

7.2.3. Relationship of Adverse Events to Study Drug

Related AEs are those for which the investigator selected "Related" on the AE case report form (CRF) to the question of "Related to Study Treatment." Events for which the investigator did not record relationships to study drug will be considered related to study drug for summary purposes. However, by-subject data listings will show the relationship as missing from that captured on the CRF.

7.2.4. Serious Adverse Events

Serious adverse events (SAEs) will be identified and captured as SAEs if AEs met the definitions of SAE specified in the study protocol. Serious adverse events captured and stored in the clinical database will be reconciled with the SAE database from the Gilead Drug Safety and Public Health Department before database finalization.

7.2.5. Treatment-Emergent Adverse Events

7.2.5.1. Definition of Treatment Emergent

Treatment-emergent adverse events (TEAEs) are defined as one or both of the following:

- Any AEs with an onset date on or after the study drug start date and no later than 30 days after permanent discontinuation of study drug.
- Any AEs leading to premature discontinuation of study drug.

7.2.5.2. Incomplete Dates

If the onset date of the AE is incomplete, then the month and year (or year alone if month is not recorded) of onset determine whether an AE is treatment emergent, as long as the AE stop date is not prior to the first dose date of study drug. The event is considered treatment emergent if both of the following 2 criteria are met:

- The AE onset and end dates are the same as or after the month and year (or year) of the first dose date of study drug
- The AE onset date is the same as or before the month and year (or year) of the 30th day after the date of the last dose of study drug

An AE with completely missing onset and stop dates, or with the onset date missing and a stop date later than the first dose date of study drug, will be considered to be treatment emergent.

7.2.6. Summaries of Adverse Events and Deaths

A brief high-level summary of TEAEs will be provided by region and by the number and percentage of subjects who had the following: any AE; any AE of Grade 3 or above; any AE of Grade 2 or above; any treatment-related AE; any treatment-related AE of Grade 3 or above; any treatment-related AE of Grade 2 or above; any SAE; any treatment-related SAE; any AE that led to premature discontinuation of SOF/VEL, any AE that led to interruption of SOF/VEL. All deaths (including those that are treatment emergent and those that are not treatment emergent) observed during the study will also be summarized and included in this table.

Adverse event summaries will provide the number and percentage of subjects with TEAEs by SOC and PT, by region based on the Safety Analysis Set as follows:

- All AEs
- AEs of Grade 3 or above
- AEs of Grade 2 or above
- All treatment-related AEs
- Treatment-related AEs of Grade 3 or above
- Treatment-related AEs of Grade 2 or above
- All SAEs
- All treatment-related SAEs
- AEs leading to premature discontinuation of SOF/VEL

- Adverse Events Leading to Interruption of SOF/VEL
- Deaths

Multiple events will be counted only once per subject in each summary. Adverse events will be summarized and listed by region first in alphabetic order of SOC and then by PT in order of descending incidence within the Overall group within each SOC. In summaries by severity grade, the most severe grade will be used for those AEs that occurred more than once in an individual subject during the study.

In addition to the above summary tables, TEAEs will be summarized by PT only and by region, in order of descending incidence in the Overall group for:

- All AEs
- AEs that occurred in at least 5% of subjects within any region
- AEs of Grade 3 or above
- All treatment-related AEs
- All SAEs
- AEs leading to premature discontinuation of SOF/VEL
- AEs leading to interruption of SOF/VEL

In addition to the summaries described above, data listings by region and subject ID (in ascending order) will be provided for the following:

- All AEs
- AEs of Grade 3 or above
- SAEs
- Deaths
- AEs leading to premature discontinuation of SOF/VEL
- Adverse Events Leading to Interruption of SOF/VEL
- AE with changes other than resolution dates between the SVR12 and SVR24 analyses (provided only at the final analysis)

7.3. Laboratory Evaluations

Laboratory data collected during the study will be analyzed and summarized using both quantitative and qualitative methods. Summaries of laboratory data will be provided for the Safety Analysis Set and will include data collected up to the last dose of study drug plus 30 days for subjects who have permanently discontinued study drug, or all available data in the database snapshot for subjects who were still on treatment at the time of an interim analysis. The analysis will be based on values reported in conventional units. When values are below the limit of quantitation, they will be listed as such, and the closest imputed value will be used for the purpose of calculating summary statistics. For example, if "< 0.2" was recorded, a value of 0.1 will be used for the purpose of calculating summary statistics; if "< 0.1" was recorded, a value of 0.09 will be used for the purpose of calculating summary statistics.

A by-subject listing for laboratory test results will be provided by region, subject ID number and visit in chronological order for hematology, serum chemistry, and urinalysis separately. Values falling outside of the relevant reference range and/or having a severity grade of 1 or higher on the Gilead Grading Scale for Severity of Adverse Events and Laboratory Abnormalities will be flagged in the data listings, as appropriate.

No inferential statistics will be generated.

7.3.1. Summaries of Numeric Laboratory Results

Descriptive statistics (n, mean, SD, median, Q1, Q3, minimum, and maximum) will be provided by region for ALT, AST, total bilirubin, alkaline phosphatase, white blood cell (WBC), neutrophils, lymphocytes, hemoglobin, platelets, reticulocytes, and INR as follows:

- Baseline values
- Values at each postbaseline visit
- Change from baseline at each postbaseline visit

A baseline laboratory value will be defined as the final assessment performed on or prior to the date/time of first dose of study drug. Change from baseline to a postbaseline visit will be defined as the visit value minus the baseline value. The mean, median, Q1, Q3, minimum, and maximum will be displayed to the reported number of digits; SD to the reported number of digits plus 1.

Median (Q1, Q3) of the observed values for ALT, AST, total bilirubin, alkaline phosphatase, hemoglobin, reticulocytes, WBC, neutrophils, lymphocytes, and platelets will be plotted using a line plot by visit and region.

In the case of multiple values in an analysis window, data will be selected for analysis as described in Section 3.7.3 (Selection of Data in the Event of Multiple Records in a Window).

The number of subjects with hemoglobin < 10 g/dL and < 8.5 g/dL at any postbaseline visits (up to 30 days after the last dose of any study drug) will be summarized by region.

7.3.2. Graded Laboratory Values

The Gilead Grading Scale for Severity of Adverse Events and Laboratory Abnormalities will be used for assigning toxicity grades (0 to 4) to laboratory results for analysis. Grade 0 includes all values that do not meet the criteria for an abnormality of at least Grade 1. Some laboratory tests have criteria for both increased and decreased levels; analyses for each direction (ie, increased, decreased) will be presented separately.

7.3.2.1. Treatment-Emergent Laboratory Abnormalities

Treatment-emergent laboratory abnormalities are defined as values that increase at least 1 toxicity grade from baseline at any postbaseline time point, up to and including the date of last dose of study drug plus 30 days for subjects who permanently discontinued study drug, or all available data in the database snapshot for subjects who were still on treatment at the time of an interim analysis. If the relevant baseline laboratory value is missing, then any abnormality of at least Grade 1 will be considered treatment emergent.

7.3.2.2. Summaries of Laboratory Abnormalities

Laboratory data that are categorical will be summarized using the number and percentage of subjects in the study with the given response at baseline and each scheduled postbaseline visit.

The following summaries (number and percentage of subjects) for treatment-emergent laboratory abnormalities will be provided by analyte and region; subjects will be categorized according to the most severe postbaseline abnormality grade for a given analyte:

- Graded laboratory abnormalities
- Grade 3 or above laboratory abnormalities

For all summaries of laboratory abnormalities, the denominator is the number of subjects with nonmissing postbaseline values up to 30 days after last dose of study drug for the laboratory parameter of interest.

A by-subject listing of treatment-emergent Grade 3 or above laboratory abnormalities will be provided by region, subject ID number and visit in chronological order. This listing will include all test results that were collected throughout the study for the analyte of interest, with all applicable severity grades or abnormal flags displayed.

A by-subject listing of medical history and prior and concomitant medications for subjects with treatment-emergent grade 3 or above laboratory abnormalities of glucose will be provided by region, subject ID number and date in chronological order.

7.4. Body Weight, Height, and Vital Signs

Vital signs (systolic and diastolic blood pressure [mmHg], pulse [beats/min]) at each visit, and change from baseline at each visit will be summarized for the Safety Analysis Set using descriptive statistics (n, mean, SD, median, Q1, Q3, minimum, and maximum) by region. The baseline value will be defined as the last available value collected on or prior to the date/time of first dose of study drug. Change from baseline to a postbaseline visit will be defined as the postbaseline value minus the baseline value.

In the case of multiple values in an analysis window, data will be selected for analysis as described in Section 3.7.3 (Selection of Data in the Event of Multiple Records in a Window). No inferential statistics will be generated.

A by-subject listing of vital signs (systolic and diastolic blood pressure [mmHg], pulse [beats/min], respiration [breaths/min], and body temperature [^{o}C]) will be provided by region, subject ID number and visit in chronological order. In the same manner, a by-subject listing of body weight, height, and BMI will be provided separately.

7.5. Prior and Concomitant Medications

Medications collected at Screening and during the study will be coded using the current version of the World Health Organization (WHO) Drug dictionary. The medications will be categorized as prior, concomitant, or both using the following definitions:

- Prior medications: any medications taken and stopped prior to or on the date of first study drug administration

- Concomitant medications: any medications taken after the date of first study drug administration and up to the last dosing date of study drug

Concomitant medications will be summarized by Anatomical Therapeutic Chemical (ATC) drug class Level 2, and preferred name using the number and percentage of subjects for each region. A subject reporting the same medication more than once will be counted only once when calculating the number and percentage of subjects who received that medication.

Summaries will be based on the Safety Analysis Set by region. No inferential statistics will be generated.

For purposes of analysis, any medication with a stop date that is on or prior to the initial study drug dosing date or a start date that is after the last study drug dosing date will be excluded from a concomitant medication summary. If a partial stop date is entered, any medication with the month and year (if day is missing) or year (if day and month are missing) prior to the initial study drug dosing date will be excluded from the concomitant medication summary. If a partial start date is entered, then any medication with the month and year (if day is missing) or year (if day and month are missing) after the study drug stop date will be excluded from the concomitant medication summary. Medications with completely missing dates will be included in the concomitant medication summary.

All prior and concomitant medications (other than per-protocol study drugs) will be provided in a by-subject listing sorted by region, subject ID number and administration date in chronological order.

7.6. Electrocardiogram Results

A shift table of the investigators' assessment of ECG results at each visit compared with baseline values will be presented by region using the following categories: normal; abnormal, not clinically significant; abnormal, clinically significant; or missing. The number and percentage of subjects in each cross-classification group of the shift table will be presented. Subjects with a missing value at baseline or postbaseline will not be included in the denominator for percentage calculation. No inferential statistics will be provided.

A by-subject listing for ECG assessment results for all subjects will be provided by region, subject ID number and visit in chronological order.

A by-subject listing for clinically significant ECG assessment results will be provided by region, subject ID number and visit in chronological order.

7.7. Other Safety Measures

A data listing will be provided for subjects who become pregnant during the study.

7.8. Changes From Protocol-Specified Safety Analyses

There are no deviations from the protocol-specified safety analyses.

8. REFERENCES

Clopper CJ, Pearson ES. The Use of Confidence or Fiducial Limits Illustrated in the Case of the Binomial. Dec. Biometrika 1934;26 (4):pp. 404-13.

Weins BL, Lystig TC, Berry SM. Recent Statistical Contributions to Medical Device Development. Therapeutic Innovation & Regulatory Science 2013:1-8.

Yu ML, Chuang WL. Treatment of chronic hepatitis C in Asia: when East meets West. J Gastroenterol Hepatol 2009;24 (3):336-45.

9. SOFTWARE

SAS® Software Version 9.4. SAS Institute Inc., Cary, NC, USA.

10. SAP REVISION

Revision Date (DD MMM YYYY)	Section	Summary of Revision	Reason for Revision

11. APPENDICES

Appendix 1. Study Procedures Table

Study Visits

	Screening	Day 1	On-treatment Study Week (± 3 days)							Post treatment Study Week (± 5 days)[i]		
			1	2	4	6	8	10	12/ET	4	12	24
Clinical Assessments												
Informed Consent	X											
Determine Eligibility	X	X										
Medical History	X											
Physical Examination	X	X							X			
Height	X											
Weight	X	X							X		X	X
Vital Signs[b]	X	X	X	X	X	X	X	X	X	X	X	X
12-Lead ECG[c]	X	X	X						X			
AEs	X	X	X	X	X	X	X	X	X	X		
Concomitant Medications	X	X	X	X	X	X	X	X	X	X		
Pregnancy Prevention Counseling		X							X	X		
Health Related Quality of Life Survey, SF-36		X							X	X	X	
Review of Study Medication Compliance[g]			X	X	X	X	X	X	X			
Study Drug Dispensing[a]		X			X		X					

	Screening	Day 1	On-treatment Study Week (± 3 days)							Post treatment Study Week (± 5 days)[i]		
			1	2	4	6	8	10	12/ET	4	12	24
Laboratory Assessments												
Hematology, Chemistry	X	X	X	X	X	X	X	X	X	X		
Coagulation Tests	X	X							X			
HCV RNA	X	X	X	X	X	X	X	X	X	X	X	X
Viral RNA Sequencing / Phenotyping Sample[j]		X	X	X	X	X	X	X	X	X	X	X
Pregnancy Testing[d]	X	X			X		X		X	X		
Urinalysis, Urine Drug Screen	X											
HCV Genotyping, IL28B	X											
HCV, HIV, HBV Serology	X											
HbA1c, Fibrotest®	X											
PPD												
Pharmacogenomic Sample[e]		X										
Imaging for Hepatocellular Carcinoma (HCC)[f]	X											

a Day 1 assessments must be performed prior to dosing.
b Vital signs include resting blood pressure, pulse, respiratory rate, and temperature.
c Subjects will be required to rest in a supine position for ≥ 5 minutes prior to making a recording. The investigator (or qualified designee) should review the ECG traces recorded in real time for gross abnormalities.
d Females of childbearing potential only. Serum β-hCG pregnancy test performed at screening and confirmation of positive urine pregnancy test. All females of childbearing potential will have urine pregnancy testing every 4 weeks during the dosing period. If urine is positive, confirm immediately with serum β-hCG.
e Only for subjects who have provided consent for this sample and testing. This sample can be obtained at a subsequent visit if not obtained at Day 1.
f If presence of cirrhosis is determined, then appropriate diagnostic imaging (e.g., CT or ultrasound) should be performed to exclude the presence of hepatocellular carcinoma (HCC)
g Subjects must be instructed to bring back all medication in the original container at every post-Day 1 study visit through the end of treatment. Study medication will be reconciled at every post-Day 1 visit by the investigator in order to monitor the subject's adherence with the medication regimen.
h PPD
i All subjects will complete Post treatment Week 4. Subjects with HCV RNA < LLOQ at the post treatment Week 4 and/or Week 12 visits will complete the subsequent post treatment visits, unless viral relapse is determined.
j Plasma samples will be collected for possible viral resistance and other Virology studies