Name of Sponsor/Company: Bristol-Myers Squibb	Individual Study Table Referring to the Dossier	*(For National Authority Use Only)*
Name of Finished Product:		
Name of Active Ingredient: NS3 Protease Inhibitor (BMS-650032)		

SYNOPSIS

Final Clinical Study Report for Study AI447016

TITLE OF STUDY: A Phase 2a/2b Study of BMS-650032 in Combination with Peginterferon alfa-2a (Pegasys®) and Ribavirin (Copegus®) in Treatment-Naive Subjects with Genotypes 1 and 4 Chronic Hepatitis C Infection

INVESTIGATORS/STUDY CENTERS: Fifteen (15) sites: 6 in France and 9 in the United States of America

PUBLICATIONS: None

STUDY PERIOD: Study Initiation Date: 09-Feb-2010

Study Completion Date: The study is ongoing. The last patient last visit for this report of Stage 1 Week 12 analysis is 27-July-2010. The data cut-off for this report of the primary endpoints (Week 12 of Stage 1) is 01-Sep-2010.

CLINICAL PHASE: 2a (Stage1) /2b (Stage 2)

OBJECTIVES:

Stage 1 primary objectives were based on Week 12 analysis of safety and antiviral activity data. The Week 12 analysis in Stage 1 supports dose selection decisions for Stage 2, while the analyses in Stage 2 will support the overall hepatitis C virus (HCV) program (add-on to pegylated interferon alfa [pegIFNα]/ribavirin [RBV] and combination antiviral studies) and inform decisions on both dose (Week 12 analysis) and duration (sustained virologic response [SVR] analysis).

Primary Objectives:

The following Stage 1 primary endpoints, based on Week 12 analysis, were used to assess safety and antiviral activity of each BMS-650032 dose relative to pegIFNα/RBV and are presented in this report:

- Safety, as measured by the frequency of serious adverse events (SAEs) and discontinuations due to adverse events (AEs);
- Antiviral activity, as determined by the proportion of HCV genotype 1 subjects with extended rapid virologic response (eRVR), defined as undetectable HCV ribonucleic acid (RNA) at both Weeks 4 and 12.

In addition, the following Stage 2 primary endpoint will be presented in an addendum to the clinical study report (CSR):

- Antiviral activity, as determined by the proportion of HCV genotype 1 subjects with 24-week sustained virologic response (SVR_{24}), defined as undetectable HCV RNA at follow-up Week 24.

Secondary Objectives:

The following Stage 1 secondary objectives are presented in this report:

- To assess the proportion of HCV genotype 1 subjects with rapid virologic response (RVR), defined as undetectable HCV RNA at Week 4;
- To assess the proportion of HCV genotype 1 subjects with early virologic response (EVR), defined as ≥ 2 $\log_{10}$ decrease in HCV RNA from baseline or HCV RNA < limit of quantitation (LOQ) at Week 12.

In addition, the following Stage 1 secondary objectives will be presented in an addendum to the CSR:

- To assess the proportion of HCV genotype 1 subjects with 12-week sustained virologic response (SVR_{12}), defined as undetectable HCV RNA at follow-up Week 12;
- To assess the proportion of HCV genotype 1 subjects with SVR_{24}, defined as undetectable HCV RNA at follow-up Week 24;
- To describe resistant variants associated with virologic failure.

Other Objectives:

The following Stage 1 exploratory objectives are presented in this report:

- To explore the relationship between antiviral activity endpoints and single nucleotide polymorphisms (SNPs) in genes encoding proteins of the interferon lambda (IFNλ) family (IL28A, IL28B, IL29);
- To evaluate antiviral activity endpoints by the Abbott RealTime assay.

In addition, the following exploratory objectives will be presented in an addendum to the CSR:

- To explore the relationship between endpoints of safety or antiviral activity and exposure to BMS-650032 when co-administered with pegIFNα/RBV;
- To describe the pharmacokinetics (PK) of BMS-650032, RBV, and pegIFNα;
- To describe the relationship between the duration of study therapy and SVR endpoints for HCV genotype 1 subjects on the BMS-650032 regimens who achieved protocol-defined response (PDR) (Stage 2 only);
- To evaluate antiviral activity endpoints for HCV genotype 4 subjects (Stage 2 only).

METHODOLOGY: This is an ongoing, comparative, randomized, multi-center, combined Phase 2a/2b study that was intended to establish safety and efficacy of at least 2 doses of BMS-650032 in combination with the standard of care (SOC) pegIFNα/RBV in Phase 2a (Stage 1), and to select 2 of the 3 doses being evaluated in Phase 2a for inclusion in Phase 2b (Stage 2).

Stage 1 is a double-blind randomized Phase 2a design of 3 doses of BMS-650032 plus pegIFNα/RBV versus placebo plus pegIFNα/RBV. Treatment-naive, genotype 1 HCV-infected subjects were randomized in a 1:1:1:1 ratio to receive BMS-650032 (200 mg twice daily (BID), or 600 mg once daily (QD), or 600 mg BID) plus pegIFNα/RBV, or placebo plus pegIFNα/RBV. The placebo regimen provided reference

data to evaluate safety and tolerability of treatment with BMS-650032 combined with pegIFNα/RBV. The site and the subject were blinded to treatment assignment throughout the study. Bristol-Myers Squibb (BMS) personnel were blinded to treatment assignment until the Week 12 interim analysis.

A blinded cohort safety analysis was performed at Week 4, and the primary endpoint was at Week 12. Based on analysis of Week 12 safety and efficacy data, 1 dose (200-mg BID BMS-650032) was selected for evaluation in Stage 2. A treatment group was to be discontinued in Stage 1 if the dose was not selected for Stage 2 because of safety concerns.

Stage 2 results will be presented in an addendum to the CSR.

NUMBER OF SUBJECTS (Planned and Analyzed): Forty-eight (48) subjects were planned to be randomized and treated during Stage 1. Forty-eight (48) subjects were randomized to receive treatment, 12 subjects in each of the BMS-650032 dose groups (200-mg BID, 600-mg BID, or 600-mg QD) and 12 in the placebo group. Of the 48 randomized subjects, 1 subject randomized into the placebo group was not treated due to pregnancy.

DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION: Adult men and women 18 to 70 years of age, with chronic HCV genotype 1 and genotype 4 (Stage 2 only) who had not received prior treatment with pegIFNα and RBV or other agents with anti-HCV activity, and who did not exhibit human immunodeficiency virus (HIV) or hepatitis B virus (HBV) co-infection or advanced liver disease were enrolled in the study.

TEST PRODUCT, DOSE AND MODE OF ADMINISTRATION, DURATION OF TREATMENT, BATCH NUMBERS: During Stage 1, subjects were administered BMS-650032 orally at doses of 200 mg BID, 600 mg BID, or 600 mg QD. Treatment was to continue for 48 weeks. Batch number for BMS-650032 film-coated 200-mg tablet used in this study was 9K52569.

REFERENCE THERAPY, DOSE AND MODE OF ADMINISTRATION, DURATION OF TREATMENT, BATCH NUMBERS: Subjects received treatment with placebo orally. Treatment was to continue for 48 weeks.

All subjects also received pegIFNα/RBV treatment for HCV infection: pegIFNα given once weekly and RBV given BID, in the morning and evening with food. Batch number for placebo film-coated tablet used in this study was 9K52555. Bristol-Myers Squibb supplied sufficient marketed pegIFNα and RBV product as follows: pegIFNα (Pegasys®) as pre-filled syringes containing 180 mcg/0.5ml, manufactured by Roche Laboratories, Inc, batch number B1149 (expiration: 30-Jun 2012); RBV (Copegus®) as 200 mg film-coated tablets manufactured by Roche Laboratories, Inc, batch number 118765 (expiration: 30-Apr-2012).

CRITERIA FOR EVALUATION:

Efficacy: The primary antiviral activity endpoint was the proportion of subjects with eRVR defined as undetectable HCV RNA at both Weeks 4 and 12. Other antiviral activity endpoints assessed in this analysis were the proportions of subjects with RVR defined as undetectable HCV RNA at Week 4; and proportion of subjects with EVR defined as ≥ 2 $\log_{10}$ decrease in HCV RNA from baseline or HCV RNA < LOQ at Week 12. Analyses were based on the Roche Taqman assay. Additional exploratory analyses were performed using the Abbott RealTime assay.

Safety: Key safety endpoints included deaths, SAE, AEs leading to discontinuation, Grade 3 or 4 AEs, Grade 2 to 4 related AEs, and Grade 3 to 4 laboratory abnormalities.

Pharmacokinetics: Determination of PK parameters of BMS-650032, RBV, and pegIFNα was part of the study design. PK results will be analyzed at study completion and results will be presented in an addendum to the CSR.

Pharmacodynamics: Single nucleotide polymorphism (SNP) samples were collected from all subjects (except at sites where collection was not feasible due to country regulations) to explore the relationship between antiviral activity endpoints and SNPs in genes encoding proteins of the IFNλ family (IL28A, IL28B, IL29).

Other: Resistant testing of variants associated with virologic failure was a secondary endpoint. Results will be analyzed at study completion and presented in an addendum to the CSR.

STATISTICAL CONSIDERATIONS:

An analysis of early safety and antiviral activity by coded treatment regimen was performed at Week 4. This unblinded analysis of safety and antiviral activity to support Phase 2b dose selection was conducted after all subjects reached Week 12. Future Stage 1 planned analyses include another unblinded analysis of safety and antiviral activity after all subjects complete 12 weeks of follow-up, and a final analysis after all subjects complete 24 weeks of follow-up. Antiviral activity analyses were based on the Roche Taqman assay. Additional exploratory analyses were performed using the Abbott RealTime assay.

Safety and antiviral activity were assessed for treated subjects using descriptive and exploratory analyses. Antiviral activity endpoints were assessed using modified intent to treat (ITT) and observed values. In both analyses, the numerator was based on subjects meeting the response criteria. For modified ITT, the denominator was based on all treated subjects. For observed values, the denominator was based on treated subjects with available HCV RNA measurements at the analysis weeek(s). Response rates were presented with 2-sided 80% exact binomial confidence intervals (CIs). Cohort safety stopping rules were assessed as described in the protocol.

SUMMARY OF RESULTS:

Disposition and Baseline/Demographic Characteristics: Forty-eight (48) subjects were randomized to receive treatment, 12 subjects in each of the BMS-650032 dose groups (200-mg BID, 600-mg BID, or 600-mg QD) and 12 in the placebo group (Table 1). Of the 48 randomized subjects, 1 subject randomized into the placebo group was not treated due to pregnancy.

Table 1: End of Week-24 Treatment Period Subject Status Summary- Treated Subjects

Number of Subjects (%)[a]	BMS-650032 200 mg BID (N = 12)	BMS-650032 600 mg BID (N = 12)	BMS-650032 600 mg QD (N = 12)	Placebo (N = 11)
Subjects completing the period	3 (25.0)	1 (8.3)	1 (8.3)	1 (9.1)
Subjects not completing the period	0	1 (8.3)	1 (8.3)	4 (36.4)
Reason for not completing the period				
Lack of efficacy	0	0	0	2 (18.2)
Adverse event[b]	0	1 (8.3)	1 (8.3)	1 (9.1)
Poor/non-compliance	0	0	0	1 (9.1)
Subjects continuing the study	3 (25.0)	1 (8.3)	2 (16.7)	4 (36.4)
Subjects not continuing the study	0	1 (8.3)	0	1 (9.1)
Reason for not continuing in the study				
Lack of efficacy	0	0	0	1 (9.1)
Adverse event[c]	0	1 (8.3)	0	0

[a] Results are shown for the 12 subjects with complete subject status CRFs, at the time of Week 12 analysis.

[b] Of the 12 subjects with complete subject status CRFs, 6 discontinued all study therapy (BMS-650032/placebo, pegIFNα, and RBV), of whom 3 discontinued all study therapy due to AEs: including Grade 1 influenza-like illness (1 subject; 600-mg BID); Grade 3 hepatic enzyme increased at Week 16 (1 subject; 600-mg QD); and Grade 3 asthenia (1 subject; placebo).

[c] Of the 6 subjects who discontinued all study therapy, 2 also discontinued the study due to lack of efficacy (1 subject in placebo group) or AE (1 subject: Grade 1 influenza-like illness for 1 subject in the 600-mg BID BMS-650032 group).

The demographic characteristics for treated subjects were balanced among the BMS-650032 and placebo groups and are summarized in Table 2. Baseline HCV disease characteristics were balanced among the BMS-650032 and placebo groups. Mean HCV RNA level as measured with the Roche assay and the Abbott assay, ranged from 6.4 to 6.8 $\log_{10}$ IU/mL and 6.0 to 6.3 $\log_{10}$ IU/mL, respectively. For all subjects, mean HCV RNA was 6.6 $\log_{10}$ IU/mL, and 79% of subjects had HCV RNA genotype 1a.

Table 2: Summary of Demographic Characteristics - Treated Subjects (Stage 1)

	BMS-650032 200 mg BID (N = 12)	BMS-650032 600 mg BID (N = 12)	BMS-650032 600 mg QD (N = 12)	Placebo (N = 11)	Total (N = 47)
Age (years)					
Mean	43.8	45.8	50.3	42.7	45.7
Standard deviation	11.90	9.97	9.18	10.34	10.48
Min, Max	21, 56	27, 55	31, 69	23, 54	21, 69
Age categorization (n, %)					
21 - < 65 years	12 (100)	12 (100)	11 (91.7)	11 (100)	46 (97.9)
≥ 65 years	0	0	1 (8.3)	0	1 (2.1)
Gender (n, %)					
Male	8 (66.7)	8 (66.7)	10 (83.3)	9 (81.8)	35 (74.5)
Female	4 (33.3)	4 (33.3)	2 (16.7)	2 (18.2)	12 (25.5)
Race (n, %)					
White	11 (91.7)	8 (66.7)	9 (75.0)	10 (90.9)	38 (80.9)
Black/African American	1 (8.3)	4 (33.3)	2 (16.7)	1 (9.1)	8 (17.0)
American Indian/Alaska native	0	0	1 (8.3)	0	1 (2.1)
Ethnicity (n, %)					
Hispanic/Latino	0	1 (8.3)	1 (8.3)	1 (9.1)	3 (6.4)
Not Hispanic/Latino	5 (41.7)	7 (58.3)	3 (25.0)	5 (45.5)	20 (42.6)
Not reported	7 (58.3)	4 (33.3)	8 (66.7)	5 (45.5)	24 (51.1)

BID = twice daily; QD = once daily

Efficacy Results: A difference in reported antiviral response rates between the Roche Taqman assay and the Abbot RealTime assay was observed at Week 4 (RVR and thus eRVR), but not for later timepoints (EVR or complete early virologic response [cEVR]). Primary and secondary antiviral activity endpoints using the Roche and Abbott assays are summarized in Table 3. A summary of undetectable HCV RNA endpoints by the Roche assay is presented in Figure 1.

Table 3: Summary of Primary and Secondary Efficacy Endpoints: Modified Intent to Treat Analysis - Treated Subjects (Stage 1)

Number of Subjects (%)	BMS-650032 200 mg BID (N = 12)	BMS-650032 600 mg BID (N = 12)	BMS-650032 600 mg QD (N = 12)	Placebo (N = 11)
Primary Antiviral Endpoint				
Extended Rapid Virologic Response[a]				
(Roche Assay)				
Responder (%)	9 (75.0)	9 (75.0)	11 (91.7)	0
80% CI	(52.5, 90.4)	(52.5, 90.4)	(71.3, 99.1)	(0.0, 18.9)
(Abbott Assay)				
Responder (%)	3 (25.0)	3 (25.0)	4 (33.3)	0
80% CI	(9.6, 47.5)	(9.6, 47.5)	(15.4, 55.9)	(0.0, 18.9)
Secondary Antiviral Endpoint				
Rapid Virologic Response[b]				
(Roche Assay)				
Responder (%)	10 (83.3)	10 (83.3)	11 (91.7)	0
80% CI	(61.4, 95.5)	(61.4, 95.5)	(71.3, 99.1)	(0.0, 18.9)
(Abbott Assay)				
Responder (%)	3 (25.0)	3 (25.0)	4 (33.3)	0
80% CI	(9.6, 47.5)	(9.6, 47.5)	(15.4, 55.9)	(0.0, 18.9)
Early Virologic Response[c]				
(Roche Assay)				
Responder (%)	12 (100)	11 (91.7)	12 (100)	11 (100)
80% CI	(82.5, 100)	(71.3, 99.1)	(82.5, 100)	(81.1, 100)
(Abbott Assay)				
Responder (%)	12 (100)	11 (91.7)	12 (100)	9 (81.8)
80% CI	(82.5, 100)	(71.3, 99.1)	(82.5, 100)	(58.5, 95.1)
Complete Early Virologic Response[d]				
(Roche Assay)				
Responder (%)	11 (91.7)	10 (83.3)	12 (100)	7 (63.6)
80% CI	(71.3, 99.1)	(61.4, 95.5)	(82.5, 100)	(40.1, 83.1)
(Abbott Assay)				
Responder (%)	10 (83.3)	11 (91.7)	10 (83.3)	6 (54.5)
80% CI	(61.4, 95.5)	(71.3, 99.1)	(61.4, 95.5)	(31.8, 75.9)

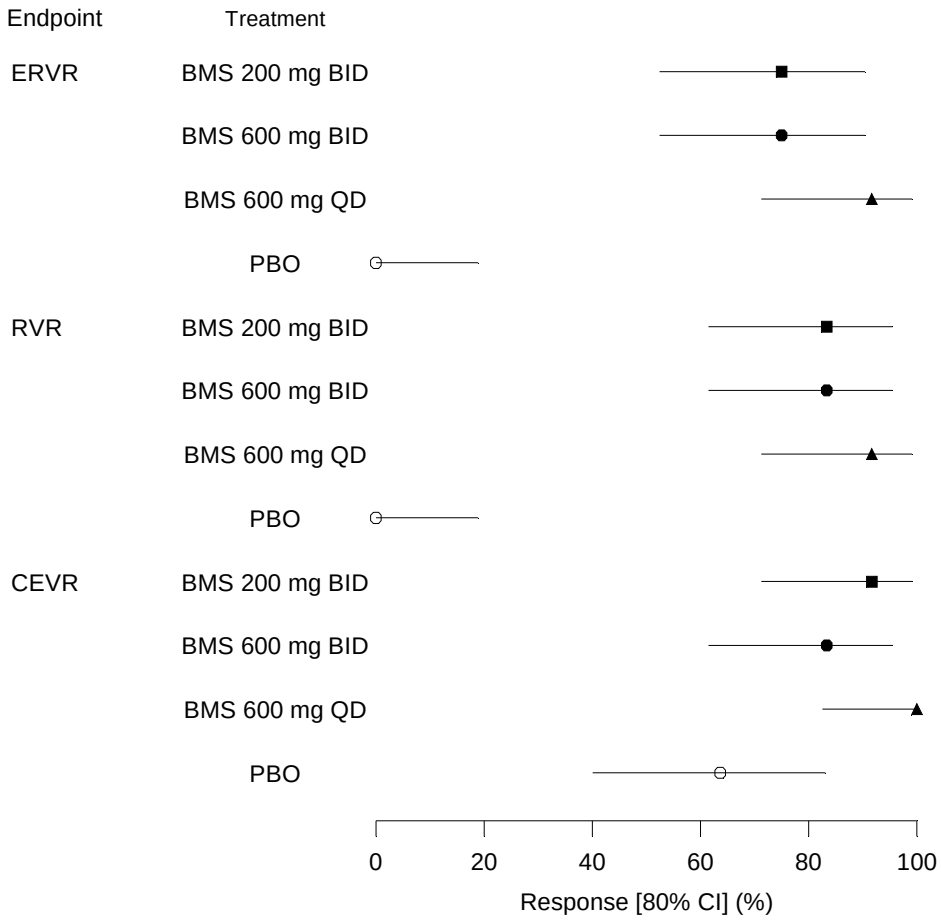
[a] Undetectable HCV RNA at both Weeks 4 and 12

[b] Undetectable HCV RNA at Week 4

[c] Defined as ≥ 2 $\log_{10}$ decrease in HCV RNA from baseline or HCV RNA < LOQ at Week 12

[d] Undetectable HCV RNA at Week 12

Figure 1: **Undetectable HCV RNA Endpoints - Roche Assay Modified ITT - Treated Subjects (Stage 1)**



N = 12 subjects per BMS treatment group, N = 11 on PBO

Program Path: /gbs/prod/clin/programs/ai/447/016/wk12/rpt/graphs
Program Name: _d-graphs.sas 13SEP2010:05:21:17

Safety Results: All treatment regimens were generally well tolerated. A summary of safety is presented in Table 4.

Table 4: Summary of Safety - Treated Subjects (Stage 1)

	Number of Subjects (%)			
	BMS-650032 200 mg BID (N = 12)	**BMS-650032 600 mg BID (N = 12)**	**BMS-650032 600 mg QD (N = 12)**	**Placebo (N = 11)**
Deaths	0	0	0	0
SAEs[a]	1 (8.3)	0	1 (8.3)	0
AEs leading to discontinuation of study therapy[b]	0	2 (16.7)	2 (16.7)	1 (9.1)
AEs through Week 12; Grade 1 - 4	12 (100)	12 (100)	11 (91.7)	10 (90.9)
Most frequently reported (≥25%) AEs				
Fatigue	3 (25.0)	5 (41.7)	10 (83.3)	3 (27.3)
Diarrhea	5 (41.7)	6 (50.0)	6 (50.0)	1 (9.1)
Influenza-like illness	4 (33.3)	3 (25.0)	6 (50.0)	4 (36.4)
Headache	4 (33.3)	3 (25.0)	3 (25.0)	6 (54.5)
Decreased appetite	4 (33.3)	4 (33.3)	4 (33.3)	3 (27.3)
Nausea	3 (25.0)	5 (41.7)	2 (16.7)	2 (18.2)
Asthenia	4 (33.3)	4 (33.3)	1 (8.3)	4 (36.4)
AEs through Week 12; Grade 3- 4[c]	0	0	2 (16.7)	3 (27.3)
Laboratory worst toxicity through Week 12; Grade 3 - 4				
Hemoglobin	0	0	2 (16.7)	0
Neutrophils + bands	1 (8.3)	2 (16.7)	2 (16.7)	2 (18.2)
WBC	0	0	1 (8.3)	0
ALT	0	1 (8.3)	1 (8.3)	0
Total bilirubin	0	0	1 (8.3)	0
Lipase	0	1 (8.3)	0	0
ALT median change from BL at Week 12 (U/L)	-8.0	0.0	10.5	-44.0

AE(s) = adverse event(s); ALT = alanine aminotransferase; BID = twice daily; BL = baseline; QD = once daily; SAE(s) = serious adverse event(s); WBC = white blood cell

[a] SAEs were reported for 2 subjects: Grade 2 abdominal pain for 1 subject in the 200-mg BID BMS-650032 group; and Grade 3 cytolytic hepatitis for 1 subject in the 600-mg QD BMS-650032 group. The event of cytolytic hepatitis led to discontinuation of BMS-650032.

[b] Five (5) subjects discontinued (any) study therapy due to AEs: 3 subjects discontinued all study drugs (BMS-650032/placebo, pegIFNα, and RBV) due to influenza like illness (1 subject; 600-mg BID BMS-650032), hepatic enzyme increase at Week 16 (1 subject; 600-mg QD BMS-650032), and asthenia (1 subject; placebo); and 2 subjects discontinued only BMS-650032 due to Grade 2 transaminases increased (1 subject; 600-mg BID BMS-650032) and Grade 3 cytolytic hepatitis (1 subject; 600-mg QD BMS-650032).

[c] Five (5) Grade 3-4 AEs were reported including: 2 (neutropenia and cytolytic hepatitis) in the 600-mg QD BMS-650032 group; and 3 (asthenia, chills, and migraine) in the placebo group.

Liver Function Tests: Alanine aminotransferase (ALT) elevations were observed with BMS-650032, which were more frequent in the 600-mg BMS-650032 regimens. Ten (10) subjects in the 200-mg BID group had normal baseline ALT values; 4 subsequently had Grade 1 to 2 ALT on-study. Seven (7) subjects in the 600-mg BID group had normal baseline ALT values; 5 subsequently had on-study Grade 1 to 2 ALT and 1 had Grade 3 to 4 ALT. Nine (9) subjects in the 600-mg QD group had normal baseline ALT values; 8 subsequently had on-study Grade 1 to 2 ALT and 1 had Grade 3 to 4 ALT. Grade 3 to 4 ALT/aspartate aminotransferase (AST) abnormalities through Week 12 were reported for 2 subjects: 1 each in the 600-mg BID and 600-mg QD dose groups.

Total bilirubin abnormalities through Week 12 were reported for 2 subjects in the 200-mg BID (Grade 1 and Grade 2 for 1 subject each), 2 in the 600-mg BID (Grade 1 and Grade 2 for 1 subject each), and 4 in the 600-mg QD (3 Grade 1; and 1 Grade 4) BMS-650032 dose groups, and 2 in the placebo group.

Pharmacogenomic Results: Although Stage 1 was small and unbalanced by HCV genotype across treatment groups, all 11 subjects with IL28B CC genotype, who received BMS-650032, achieved cEVR and RVR (Table 5). High response rates (57.1 - 100%) were also observed for non-CC subjects. In the placebo group, 1/2 of subjects with IL28B CC genotype achieved cEVR and none (0/2) achieved RVR or eRVR. The IL28B SNP genotypes of the highest frequency were: RS10853727 TT (80.9%); RS12979860 CT (51.1%); RS8103142 CT (51.1%); RS8099917 TT (48.9%); RS7248668 GG (46.8%); and RS8109886 AA (44.7%).

Table 5: Virologic Responses by *IL28B* Genotype (SNP RS12979860) (Stage 1)

Response	*IL28B* Genotype	BMS-650032 200 mg BID (N = 12)	BMS-650032 600 mg BID (N = 12)	BMS-650032 600 mg QD (N = 12)	Placebo (N = 11)
cEVR, n/N (%)	CC	5/5 (100)	1/1 (100)	5/5 (100)	1/2 (50.0)
	CT/TT	6/7 (85.7)	9/11 (81.8)	7/7 (100)	6/9 (66.7)
RVR, n/N (%)	CC	5/5 (100)	1/1 (100)	5/5 (100)	0/2
	CT/TT	5/7 (71.4)	9/11 (81.8)	6/7 (85.7)	0/9
eRVR, n/N (%)	CC	5/5 (100)	1/1 (100)	5/5 (100)	0/2
	CT/TT	4/7 (57.1)	8/11 (72.7)	6/7 (85.7)	0/9

BID = twice daily; cEVR = complete early virologic response; eRVR = extended rapid virologic response; QD = once daily; RVR = rapid virologic response; SNP = single nucleotide polymorphism

CONCLUSIONS:

- All treatment regimens were generally well tolerated and the AE profile was consistent with pegIFNα and RBV. No unique adverse events were identified for BMS-650032. Diarrhea was reported more frequently in all BMS-650032 dose groups compared to placebo; diarrhea episodes were mostly mild in intensity and did not lead to discontinuation.
- Antiviral activity of BMS-650032, as demonstrated by the proportion of subjects with eRVR (undetectable HCV RNA at Weeks 4 and 12) were comparable across BMS regimens, and higher than placebo.
- The most common Grade 3-4 laboratory abnormality was neutropenia, which is an expected event with pegIFNα/RBV, and the rate of this event was balanced across treatment regimens.
- No clinically significant difference in hemoglobin, neutrophil, platelet, or lymphocyte levels were observed in the BMS-650032 treatment groups. The changes in these laboratory values were consistent with pegIFNα/RBV therapy and did not lead to study discontinuation.

- ALT/AST elevations with or without total bilirubin elevations were more frequent in the BMS-650032 treatment groups relative to the placebo arm. Elevations were more prominent at the two 600-mg dose levels (BID and QD) than the 200-mg BID dose.
- Extended rapid virologic response (eRVR) rates were higher with the Roche assay than with the Abbott assay for BMS-650032 regimens. However, cEVR rates (undetectable HCV RNA at Week 12) were comparable between assays for the BMS-650032 regimens.
- Based on the efficacy and safety results from this Week 12 primary analysis, all subjects in Stage 1 will receive 200 mg BID BMS-650032 (or placebo) and only 200 mg BID BMS-650032 will be studied in Stage 2.

DATE OF REPORT: 18-May-2011