Bristol-Myers Squibb Company

Pipeline Asset Update for BMS-790052 (NS5A inhibitor) and BMS-650032 (NS3 inhibitor)

Pipeline Asset:	BMS-790052 is an NS5A inhibitor and BMS-650032 is an NS3 protease inhibitor, both in development for the treatment of chronic hepatitis C virus (HCV) infection
Current Phase of Development:	Phase II
Meeting or Publication:	American Association for the Study of Liver Diseases (AASLD) 2010
Study Title:	Combination therapy with BMS-790052 and BMS-650032 alone or with pegylated interferon and ribavirin (pegIFNα/RBV) results in undetectable HCV RNA through 12 weeks of therapy in HCV genotype 1 null responders
Abstract Number:	LB-8
Date/Time of Presentation:	November 1, 2010 from 8 a.m. – 5:30 p.m. EDT
Media Embargo:	Per AASLD press guidelines, these data are no longer under embargo.
Study Objective:	To assess the safety and antiviral activity of BMS-790052 and BMS-650032 alone or combined with pegIFNα/RBV in patients with HCV genotype 1 who have not responded to prior standard of care treatment (null responders)
Study Conclusion:	Seven out of 11 patients receiving BMS-790052 and BMS-650032 without pegIFNα/RBV achieved rapid virologic response, defined as undetectable viral load by week 4. However, viral breakthrough occurred in six of the 11 patients in this treatment group. Nine out of 10 patients receiving the combination of BMS-790052, BMS-650032 and pegIFNα/RBV achieved complete early virologic response (cEVR), defined as undetectable viral load by week 12. Adverse events were mainly mild to moderate in severity. There was no discontinuation of BMS study drugs due to adverse events.
Efficacy Results:	Patients in Group A were treated with BMS-790052 and BMS-650032. Patients in Group B were treated with BMS-790052, BMS-650032 and pegIFNα/RBV. The response rates for both treatment groups are as follows.

Response Rates	Group A n=11 (%)	Group B n=10 (%)
RVR – undetectable viral load (HCV RNA <10 IU/mL) at week 4	7 (64)	6 (60)
eRVR - undetectable viral load at both weeks 4 and 12	4 (36)	6 (60)
cEVR - undetectable viral load by week 12	5 (46)	9 (90)*
Viral breakthrough**	6/11 (55)	0

* One patient in Group B did not meet cEVR; however, on retesting the patient's viral load was undetectable.

** Viral breakthrough was defined as a) any increase in HCV RNA ≥1 $\log_{10}$ from nadir, or b) any detectable HCV RNA >25 IU/mL on or after week 4, or c) any detectable HCV RNA <25 IU/mL on or after week 4 confirmed by retesting.

Adverse Events: Two patients experienced a severe (Grade 3 or 4) adverse event – one patient in Group A experienced fatigue and one patient in Group B experienced low white blood cell count (neutropenia). There was no discontinuation of BMS study drugs due to adverse events (AEs).

AEs were mainly mild to moderate in severity. The most common AEs (more than three occurrences) across both study groups were:

Adverse Event	Group A (n=11)	Group B (n=10)
Diarrhea	8 (73%)	7 (70%)
Fatigue	6 (55%)	7 (70%)
Headache	5 (46%)	5 (50%)
Nausea	2 (18%)	5 (50%)
Cough	2 (18%)	2 (20%)
Dizziness	2 (18%)	2 (20%)
Shortness of breath (dyspnea)	2 (18%)	2 (20%)
Insomnia	2 (18%)	2 (20%)
Fever (pyrexia)	3 (27%)	1 (10%)

BMS-790052 and BMS-650032 Background: BMS-790052 is an investigational, first-in-class, highly selective oral hepatitis C NS5A inhibitor. BMS-650032 is an investigational, highly selective oral hepatitis C NS3 protease inhibitor. Both NS5A and NS3 are essential components for HCV replication.

BMS-790052 and BMS-650032 are two of several molecules Bristol-Myers Squibb is studying for the potential treatment of chronic hepatitis C. The portfolio of investigational compounds, which also

includes a novel pegylated interferon lambda, fits into the company's overall R&D focus on diseases where there is major unmet medical need.

Study Background:

This open-label, Phase IIa study enrolled hepatitis C genotype 1 patients whose virus did not respond to prior treatment with pegIFNα/RBV (null responders).

The 21 patients in this study were randomized to one of two treatment groups.

- Patients in Group A (n=11) were treated with a combination of BMS-790052 60 mg once daily and BMS-650032 600 mg twice daily, both taken orally.
- Patients in Group B (n=10) were treated with BMS-790052 60 mg once daily and BMS-650032 600 mg twice daily, in combination with pegylated interferon alpha 180 μg once weekly and ribavirin 1000-1200 mg daily in two divided doses according to body weight.

Inclusion Criteria:

- Chronic HCV infection, genotype 1
- Null responders (<2 $\log_{10}$ decline in HCV RNA following 12 weeks of treatment with pegIFN/RBV)
- HCV RNA levels $\geq 10^5$ IU/mL
- FibroTest score of ≤0.72 and APRI ≤2 *or* documented liver biopsy within 12 months showing absence of cirrhosis

Exclusion Criteria:

- HCV-infected patients who are treatment intolerant
- Pregnant or breastfeeding women
- Any of the following laboratory results at screening or prior to dosing:
    - Hemoglobin ≤12 g/dL for women and ≤3 g/dL for men
    - ANC ≤1500/μL
    - Platelet count ≤90,000/μL
    - ALT >5x ULN
    - Direct bilirubin >1.5x ULN
    - Albumin <3.2 g/dL
    - Creatinine clearance <50 mL/min

ClinicalTrials.gov Identifier:

NCT01012895

Request for More Information and Media Interviews:

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Supporting Information:

The abstract can be viewed on the AASLD website.