First Hepatitis C Treatment Data Demonstrating Proof of Principle with Direct-Acting Antiviral-only Therapy Published

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Study also Demonstrated 100% Sustained Virologic Response 12-Weeks Post Treatment with Quadruple Therapy

**Phase II Investigational Data Published Today in the New England Journal of Medicine**

PRINCETON, N.J.--(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE: BMY) today announced the full results, published in the New England Journal of Medicine, from a Phase II clinical trial in patients with hepatitis C virus (HCV) genotype 1 who had not responded to prior therapy with PEG-interferon alfa and ribavirin (‘null responders’). The study demonstrated that its primary endpoint of the achievement of sustained virologic response 12-weeks post-treatment (SVR12) is possible with a direct-acting antiviral (DAA)-only combination containing daclatasvir and asunaprevir (4/11 patients, including two of two patients infected with HCV genotype 1b). This study was the first study to demonstrate the possibility that hepatitis C can be cured (defined as sustained virologic response 48 weeks post-treatment or SVR48) without the use of interferon. The study also demonstrated that 100 percent (10/10) of these difficult-to-treat patients dosed with quadruple therapy containing daclatasvir and asunaprevir in combination with PEG-Interferon alfa and ribavirin achieved SVR12.

In this study there were no serious adverse events on treatment or discontinuations due to adverse events. Diarrhea was the most common adverse event in both groups (73% and 70%).

“Even with the recent approval of two protease inhibitors, treatment of hepatitis C patients who have not responded to PEG-interferon alfa and ribavirin has limited success. Because of this high unmet medical need, there is a necessity for new combination regimens that can increase response rates in null responders,” said lead investigator Anna Lok, MD, FRCP, director of clinical hepatology and professor in the department of internal medicine at the University of Michigan Medical School in Ann Arbor. “The data seen in this study with Bristol-Myers Squibb’s investigational DAAas daclatasvir and asunaprevir, either as DAA-only therapy or as part of quadruple therapy, are encouraging as we work to advance hepatitis C therapy for this difficult-to-treat patient population. This study also shows for the very first time that sustained viral responses can be achieved without the use of interferon and ribavirin.”

Daclatasvir is the first NS5A replication complex inhibitor to be investigated in HCV clinical trials and is currently in Phase III development. Asunaprevir is an investigational, oral, selective NS3 protease inhibitor.

**Study Results**

**Viral Response: Dual DAA Therapy with daclatasvir and asunaprevir (Group A)**

Eleven patients were randomized to receive dual DAA therapy for 24 weeks. Seven of the 11 patients (64%) in Group A achieved undetectable viral load by week four, and five patients remained undetectable at the end of treatment. Of these 11 patients, one patient relapsed at four (4) weeks post treatment while four patients (36%) had sustained virological response at 12 weeks post-treatment (SVR12). In follow-up to 48-weeks post treatment, no additional cases of viral relapses were observed.

Six patients, all with HCV genotype 1a, experienced viral breakthrough on dual DAA therapy, and analysis of HCV sequences following breakthrough confirmed resistance to both antivirals. With the addition of PEG-interferon alfa and ribavirin to their regimen (rescue therapy), four of the six patients achieved undetectable viral load. Two of these patients relapsed following the treatment period and two remained undetectable, one with 14 weeks and one with 42 weeks of post treatment follow-up. Two of the six patients did not achieve undetectable HCV RNA and treatment was discontinued.

**Viral Response: Quadruple Therapy with daclatasvir, asunaprevir and PEG-Interferon alfa and ribavirin (Group B)**

Ten patients were randomized to receive quadruple therapy for 24-weeks. Six of the 10 patients (60%) in Group B achieved undetectable HCV RNA by week four. Ten of the 10 patients (100%) were undetectable by the end of treatment, and all 10 achieved SVR12. No patients experienced viral relapse during 48 weeks of post-treatment observation.
Safety

In the study, there were no serious adverse events on treatment, no deaths, and no treatment discontinuations due to adverse events. Most adverse events were mild to moderate, and the most common AEs were diarrhea (group A: 8/11, 73%; group B: 7/10, 70%), fatigue (group A: 6/11, 55%; group B: 7/10, 70%), headache (group A: 5/11, 45%; group B: 5/10, 50%), and nausea (group A: 2/11, 18%; group B: 5/10, 50%).

Six patients (four from group A, including two receiving rescue therapy, and two from group B) experienced elevated liver enzymes [ALT >3x upper limit of normal (ULN)] which did not require treatment discontinuation or dose interruptions, and all patients stabilized or improved with continued therapy. Six patients, all of whom received PEG-interferon alfa and ribavirin, experienced Grade 3 or 4 neutropenia, a blood disorder characterized by an abnormally low number of white blood cells.

About the Study

This open-label, phase IIa study evaluated the antiviral activity and safety of the combination of daclatasvir and asunaprevir with and without PEG-Interferon alfa and ribavirin in 21 HCV genotype 1 null responders. Patients in the study were randomized to receive one of two treatment regimens for 24 weeks. The 11 patients in Group A received dual-DAA therapy with daclatasvir 60 mg once daily and asunaprevir 600 mg twice daily, both taken orally. The 10 patients in Group B received quadruple therapy with daclatasvir 60 mg once daily, asunaprevir 600 mg twice daily, PEG-interferon alfa 180 µg once weekly, and ribavirin 1000-1200 mg daily (according to body weight) in two divided doses. The primary study objective was to determine the proportion of patients achieving undetectable viral load (HCV RNA <10 IU/mL) 12 weeks post-treatment (SVR12). This dual-DAA combination is now in Phase III development.

About Bristol-Myers Squibb's Commitment to Liver Disease

Bristol-Myers Squibb is advancing a portfolio of compounds that aims to address unmet medical needs across the liver disease continuum, including hepatitis C, hepatitis B and liver cancer. The Company's hepatitis C pipeline includes a portfolio of compounds with different mechanisms of action, pursuing both biologics as well as small molecule antivirals. These compounds are being studied as part of multiple novel treatment regimens with the goal of increasing SVR rates across diverse patient types and geographies. Discovered by Bristol-Myers Squibb through a genomics approach, daclatasvir, also known as BMS-790052, is the first NSSA replication complex inhibitor to be investigated in hepatitis C clinical trials and is currently in Phase III development. Asunaprevir, also known as BMS-650032, is an NS3 protease inhibitor in Phase III development for hepatitis C.

About Hepatitis C

Hepatitis C is a virus that infects the liver and is transmitted through direct contact with infected blood and blood products. An estimated 170 million people worldwide are infected with hepatitis C, with genotype 1 being the most prevalent genotype. Up to 90 percent of those infected with hepatitis C will not clear the virus and will become chronically infected. Twenty percent of people with chronic hepatitis C will develop cirrhosis and, of those, up to 25 percent may progress to liver cancer. Although there is no vaccine to prevent hepatitis C, it is a potentially curable disease.

About Bristol-Myers Squibb

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information, please visit http://www.bms.com or follow us on Twitter at http://twitter.com/bmsnews.

Bristol-Myers Squibb Forward Looking Statement

This press release contains “forward-looking statements” as that term is defined in the Private Securities Litigation Reform Act of 1995, regarding the research, development and commercialization of pharmaceutical products. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Among other risks, there can be no guarantee that the compound described in this release will move from exploratory development into full product development, that clinical trials of this compound will support a regulatory filing, or that the compound will receive regulatory approval or become a commercially successful product. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb’s business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb’s Annual Report on Form 10-K for the year ended December 31, 2010, in our Quarterly Reports on Form 10-Q, and our Current Reports on Form 8-K. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise.

1 Null responders – patients whose virus did not respond to prior treatment with PEG-interferon alfa and ribavirin (HCV RNA decrease <2 log_{10} at 12 weeks).

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