Four-Year Data Demonstrate Continued Low Incidence of BARACLUDE® (entecavir) Resistance in Nucleoside-naive Chronic Hepatitis B Patients

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Higher Rates of BARACLUDE Resistance Seen in Lamivudine-Refractory Patients

PRINCETON, N.J.--(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE: BMY) today announced new results of the BARACLUDE® (entecavir) resistance monitoring program, which found a continued low incidence of resistance in studies of nucleoside-naive chronic hepatitis B patients through four years of treatment (n=663). In the three nucleoside-naive studies analyzed, two patients, or less than one percent, experienced virologic breakthrough due to BARACLUDE resistance through the third year, and no additional patients developed resistance in the fourth year. In lamivudine-refractory patients, virologic breakthrough due to BARACLUDE resistance occurred in 15 percent (n=8/53) of patients during year four. The study results were presented today at the 42nd Annual Meeting of the European Association for the Study of Liver Diseases (EASL) in Barcelona, Spain.

Drug resistance occurs when a virus mutates to avoid the effects of the medication. This can make treatment of hepatitis B challenging, because it can decrease the efficacy of the current medication and may compromise future treatment options. To date, studies have shown that multiple mutations are required to develop BARACLUDE resistance.

“The low incidence of resistance seen in nucleoside-naive patients through four years of treatment reflects BARACLUDE's high barrier to resistance in this patient population,” said Richard Colonno, Ph.D., vice president for virology drug discovery at Bristol-Myers Squibb.

About the Analysis

More than 700 patients across six studies initiated therapy on BARACLUDE® (entecavir) and were monitored for treatment response and resistance.

The year four analysis evaluated those patients who received treatment with BARACLUDE during the fourth year (n=120 for patients in nucleoside-naive studies and n=53 for patients in lamivudine-refractory studies). In this comprehensive analysis, all patients enrolled in Bristol-Myers Squibb clinical trials ETV-014, -015, -022, -027, -026 and -901 who experienced a virologic breakthrough (greater than or equal to one log increase in HBV DNA from nadir as measured by a common assay - polymerase chain reaction or PCR), or whose virus had not yet reached undetectable levels - a measurement of the levels of hepatitis B virus in the blood (HBV DNA levels >300 copies/mL by PCR assay) at weeks 48, 96, 144, 192 or end of dosing were sequenced to determine if any changes occurred in the genetic code of the virus that would result in resistance or loss of effectiveness of BARACLUDE.

Viral load reduction in chronic hepatitis B patients treated with BARACLUDE in nucleoside-naive and lamivudine-refractory studies was also evaluated.

Data Results

The incidence of BARACLUDE resistance in patients in nucleoside-naive studies over time is low, with less than one percent of patients experiencing virologic breakthrough due to BARACLUDE resistance through four years.

* Virologic breakthrough due to BARACLUDE resistance (rtS202G) occurred in one patient out of 663 treated during the first year, who had lamivudine resistance (rtM204I) at the time of study entry and was initiated on 0.5 mg.

* No additional virologic breakthroughs due to BARACLUDE resistance were observed during the second year of treatment.

* Virologic breakthrough due to BARACLUDE resistance occurred in one additional patient out of 149 treated during the third year of treatment.

* No additional virologic breakthroughs due to BARACLUDE resistance were observed during the fourth year of treatment.

The emergence of resistance increased over four years in patients in lamivudine-refractory studies.
* Virologic breakthrough due to resistance occurred in one percent (2/187) of patients during the first year of treatment.

* Virologic breakthrough due to BARACLUDE resistance occurred in an additional ten percent (14/146) of patients during the second year of treatment.

* Virologic breakthrough due to BARACLUDE resistance occurred in an additional 16 percent (13/80) of patients during the third year.

* Virologic breakthrough due to BARACLUDE resistance occurred in an additional 15 percent (8/53) of patients during the fourth year.

* The results in these patients in years one through four were consistent with the finding that the pre-existence of lamivudine-resistant substitutions resulted in an increase in the emergence of BARACLUDE resistance.

About BARACLUDE® (entecavir)

Discovered at Bristol-Myers Squibb, BARACLUDE® (entecavir) is a nucleoside analogue indicated for the treatment of chronic hepatitis B virus infection in adults with evidence of active viral replication with either evidence of persistent elevations in serum aminotransferases (ALT or AST) or histologically active disease. BARACLUDE has been approved in more than 60 countries and regions around the world.

Important Information About BARACLUDE® (entecavir) 0.5mg/1mg Tablets

BARACLUDE® (entecavir) is a prescription medicine used for chronic infection with hepatitis B virus (HBV) in adults where the virus is multiplying and damaging the liver. BARACLUDE does not cure HBV or stop the spread of HBV to others.

People should not take BARACLUDE if they are allergic to it or any of its ingredients. BARACLUDE has not been studied in children and is not recommended for anyone less than 16 years of age.

People taking BARACLUDE should tell their healthcare provider right away if they feel very weak or tired, have unusual muscle pain, have trouble breathing, have stomach pain with nausea and vomiting, feel cold -- especially in their arms and legs, feel dizzy or lightheaded, or have a fast or irregular heartbeat, as they may be signs of a serious condition called lactic acidosis (buildup of an acid in the blood).

Lactic acidosis is a medical emergency and must be treated in the hospital. Some people who have taken medicines like BARACLUDE have developed serious liver problems called hepatotoxicity. This may occur with liver enlargement (hepatomegaly) and fat in the liver (steatosis).

People should call their healthcare provider right away if they get any of the following signs of liver problems: yellowing (jaundice) of the skin or the white part of the eyes, darkening of the urine, lightening in the color of bowel movements (stools), not feeling like eating food for several days or longer, feeling sick to the stomach (nausea), or having lower stomach pain. Lactic acidosis and hepatotoxicity have happened in some people taking medicines like BARACLUDE.

In some people, hepatitis B symptoms may get worse or become very serious when they stop taking BARACLUDE. People should not stop BARACLUDE without talking to their healthcare provider. Healthcare providers will need to follow their patients and do blood tests to check the liver when BARACLUDE is stopped. People should tell their healthcare provider if they have or develop kidney problems because their healthcare provider may want to do tests to see if a lower dose is needed or a different dose schedule.

Because BARACLUDE® (entecavir) is removed from the body through the kidneys, a lower dose or a different dose schedule may be required. Healthcare providers may want to perform tests to determine whether a patient needs a lower dose or should take BARACLUDE less often than once a day.

It is not known if BARACLUDE is safe to use during pregnancy. It is not known if BARACLUDE helps to prevent a pregnant mother from passing HBV to her baby. A pregnant woman and her healthcare provider will need to decide if BARACLUDE is right for her. A woman should not breastfeed if she is taking BARACLUDE.

People should discuss with their healthcare provider all prescription and non-prescription medicines, vitamins, herbal supplements, and other health preparations they are taking or plan to take. BARACLUDE may interact with medicines that leave the body through the kidneys. The most common side effects of BARACLUDE in clinical studies were headache, tiredness, dizziness, and nausea.

This list of side effects is not complete at this time because BARACLUDE is still under study. People should report any new or continuing symptom to their healthcare provider. BARACLUDE should be taken once daily on an empty stomach (at least two hours after a meal and two hours before the next meal). To learn more about BARACLUDE and for Full Prescribing Information, including boxed WARNINGS, please visit http://www.bms.com/.

Bristol-Myers Squibb is a global pharmaceutical and related health care products company whose mission is to extend and enhance human life.

BARACLUDE® (entecavir) is a trademark of Bristol-Myers Squibb Company.

Full prescribing information for BARACLUDE, including boxed WARNINGS, is available at http://www.bms.com/.

Web site: http://www.bms.com/

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