BARAACLE® (entecavir) Data Continue to Demonstrate Low Incidence of Resistance Through Five Years of Treatment in Nucleoside-naive Chronic Hepatitis B Patients

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- Data Indicate Pre-existing Lamivudine Resistance Predisposes Patients to Higher Rates of BARAACLE Resistance -

PRINCETON, N.J.--(BUSINESS WIRE)--New BARAACLE® (entecavir) data presented today demonstrated a continued low incidence of resistance in nucleoside-naive patients through five years of treatment. In the nucleoside-naive chronic hepatitis B patients analyzed, no additional patient developed resistance in the fifth year (n=108). Through five years of treatment, the cumulative probability of developing mutations in the virus that confer resistance to BARAACLE (also called genotypic resistance) was 1.2 percent. Bristol-Myers Squibb Company (NYSE: BMY) announced the results at the 18th Conference of the Asia-Pacific Association for the Study of the Liver (APASL) in Seoul, Korea.

In lamivudine-refractory patients who received BARAACLE after treatment with lamivudine failed, the cumulative probability of genotypic BARAACLE resistance was 51 percent through the fifth year. This finding is consistent with prior observations that the pre-existence of lamivudine-resistant mutations results in an increase in the rate of BARAACLE resistance.

“Many chronic hepatitis B patients require long-term treatment. Unfortunately, the initial benefits of therapy can be lost after the development of resistance. These five-year BARAACLE data that demonstrate long-term minimal resistance at 1.2 percent in nucleoside-naive patients can be of great importance for patients,” said Professor Ching-Lung Lai, Chief, Division of Gastroenterology and Hepatology, University of Hong Kong.

Drug resistance occurs when the hepatitis B virus (HBV) mutates, thereby avoiding the effects of the medication. This 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 BARAACLE® (entecavir) resistance.

“These long-term BARAACLE data continue to support the observations seen in the first years of treatment and are reflective of BARAACLE’s high genetic barrier to resistance,” said Helena Brett-Smith, M.D., Group Director of Clinical Research at Bristol-Myers Squibb. “More importantly, we believe the data support BARAACLE as an important initial treatment choice for chronic hepatitis B, which is a disease that results in a large global health burden.”

About the Analysis

More than 700 patients across six studies initiated therapy on BARAACLE and were monitored for treatment response and resistance.

The year five analysis expands upon previous analyses, adding in information on patients who received treatment with BARAACLE during the fifth year of follow-up (n=108 for patients in nucleoside-naive studies and n=33 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(1) or whose virus had not yet reached undetectable levels(2) at weeks 48, 96, 144, 192, 240 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 BARAACLE.

Nucleoside-naive patients in this analysis were initially treated with BARAACLE 0.5 mg in studies ETV-022 and -027 and continued treatment with BARAACLE 1 mg by enrolling in study ETV-901 with a treatment gap of less than or equal to 35 days. Lamivudine-refractory patients in this analysis initiated therapy on BARAACLE 1 mg in studies ETV-014, -015, and -026 and continued treatment in study ETV-901 with a treatment gap of less than or equal to 35 days.

Viral load reduction in chronic hepatitis B patients treated with BARAACLE® (entecavir) in nucleoside-naive and lamivudine-refractory studies was also evaluated.

Data Results

Results from these studies prior to this year five analysis were previously announced on April 14, 2007.
Nucleoside-naive data

-- The incidence of BARACLUDE resistance in patients in nucleoside-naive studies over time is low, with a cumulative probability of genotypic BARACLUDE resistance of 1.2 percent through five years.

-- No nucleoside-naive patient developed resistance (n=108) in year five.

-- 93 percent of the nucleoside-naive patients taking BARACLUDE were able to achieve and maintain an undetectable viral load (HBV DNA <300 copies/mL) through year five (n=108).

Lamivudine-refractory data

-- The results in lamivudine-refractory patients in years one through five were consistent with the finding that the pre-existence of lamivudine-resistant substitutions resulted in an increase in the emergence of BARACLUDE resistance, with a cumulative probability of genotypic resistance of 51 percent through five years.

-- In year five, 43 percent of lamivudine-refractory patients had virologic breakthrough with BARACLUDE resistance (n=33).

-- During this resistance monitoring program, 72 of the 187 lamivudine-refractory patients achieved undetectable viral load (<300 copies/mL) and of these, three patients subsequently developed genotypic resistance to BARACLUDE.

Indication and Important Safety Information About BARACLUDE® (entecavir) 0.5 mg/1 mg 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.

For people taking BARACLUDE who have or get HIV (the virus that can cause AIDS) and are not taking medicines for HIV at the same time, some HIV treatments that they may take in the future may be less likely to work. People are advised to get an HIV test before starting to take BARACLUDE and anytime that there is a chance they were exposed to HIV. BARACLUDE will not help HIV infection.

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.

Because BARACLUDE® (entecavir) is removed from the body through the kidneys, a dose adjustment 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 safety and effectiveness of BARACLUDE in liver transplant recipients is unknown. 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 biopharmaceutical and related health care products company whose mission is to extend and enhance human life. Visit Bristol-Myers Squibb at http://www.bms.com/.

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(1) Virologic breakthrough is defined as a greater than or equal to 1 log increase in HBV DNA from nadir, as measured by the polymerase chain reaction or PCR assay.
(2) Undetectable viral load is defined as HBV DNA levels less than 300 copies/mL, as measured by PCR assay.

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