CASTLE Study Showed Similar Efficacy Between Once-Daily REYATAZ® (atazanavir sulfate)/ritonavir and Twice-Daily lopinavir/ritonavir at 48 Weeks in Previously Untreated HIV-Infected Adult Patients

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Data also showed differences in gastrointestinal and lipid effects between REYATAZ/ritonavir and lopinavir/ritonavir among study population

PRINCETON, NJ—BUSINESS WIRE—Bristol-Myers Squibb Company (NYSE: BMY) today announced results from the CASTLE study, in which 300 mg of once-daily REYATAZ® (atazanavir sulfate) taken with 100 mg of ritonavir (REYATAZ/r) showed similar antiviral efficacy to twice-daily lopinavir 400 mg and ritonavir 100 mg (lopinavir/r) in previously untreated adult HIV-1 infected patients at 48 weeks, as part of HIV combination therapy. In this study, 78 percent of the 440 patients in the REYATAZ/r arm met the primary endpoint of achieving undetectable viral load (defined as HIV-1 RNA less than 50 copies/ml) at 48 weeks, compared with 76 percent of the 443 patients in the lopinavir/r arm.

CASTLE is the first large-scale, open-label, randomized study designed to demonstrate the non-inferiority of REYATAZ/r to lopinavir in previously untreated HIV-1 infected adult patients. Data from the CASTLE study were presented for the first time at the 15th Conference on Retroviruses and Opportunistic Infections (CROI) this week in Boston, Mass.

"The CASTLE study provides important additional data to inform the use of a once-daily regimen including REYATAZ and ritonavir in antiretroviral naive HIV-infected patients," said Jean-Michel Molina, M.D., Hospital Saint Louis, Paris, France. "When choosing a treatment in previously untreated patients it is important to ensure antiviral activity as well as tolerability to optimize the management of HIV infection over the long term."

The most common grade 2-4 adverse events occurring in more than two percent of patients in the once-daily REYATAZ/r arm were diarrhea (two percent and eleven percent, respectively), nausea (four percent and eight percent, respectively), jaundice (four percent and zero percent, respectively) and rash (three percent and two percent, respectively).

The REYATAZ/r arm was associated with significantly lower increases from baseline to lopinavir/r in total cholesterol, triglycerides and non-HDL cholesterol at 48 weeks (p<0.0001). Two percent of patients in the REYATAZ/r arm and seven percent of patients in the lopinavir/r arm required initiation of lipid-lowering therapy in the study.

Safety events in this study were consistent with prior experience. Four deaths were reported in each treatment arm at 48 weeks; none were attributed to the study medications. Twelve percent of patients in the REYATAZ/r arm and ten percent of patients in the lopinavir/r arm experienced a serious adverse event.

Nine percent of patients in the REYATAZ/r arm and fifteen percent of patients in the lopinavir/r arm discontinued the study therapy before week 48.

About the CASTLE Study

The international, multi-center, open-label, 96-week CASTLE study randomized 883 treatment-naive patients infected with HIV-1. Four hundred and forty patients were randomized to receive REYATAZ 300 mg and ritonavir 100 mg once daily and 443 patients were randomized to receive lopinavir 400 mg and ritonavir 100 mg twice daily, each in combination with a once-daily, fixed-dose combination of emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg. All patients had a baseline viral load of greater than or equal to 5,000 copies/ml, there was no CD4+ cell count restriction for study entry. The primary endpoint for the study was the proportion of patients with viral load of less than 50 copies/ml at 48 weeks.

Additional Study Results

A number of secondary endpoints were also measured with regard to efficacy, lipid effects, safety and tolerability. Additional study results include:

- Achievement of Undetectable Viral Load in Patients with High Baseline Viral Load: * In the study, 74 percent of the 223 patients with high baseline viral load (greater than or equal to 100,000 copies/ml) achieved undetectable viral load (less than 50 copies/ml) at 48 weeks.
- A prespecified descriptive analysis of virologic response rates (HIV-1 RNA less than 50 copies/ml) by baseline CD4+ categories (greater than 200 cell/mm3, between 100 and 200 cell/mm3, between 50 and 100 cell/mm3, and less than 50 cell/mm3) indicated that response rates were consistent across all baseline CD4+ categories in the REYATAZ/r arm. This descriptive analysis indicated that response rates were reduced for subjects with lower CD4+ counts in the lopinavir/r arm. A post hoc analysis showed no association between virologic response rates and CD4+ category within the REYATAZ/r arm (p = 0.51) and a statistically significant association between virologic response rates and CD4+ category within the lopinavir/r arm (p = 0.0005).

About REYATAZ® (atazanavir sulfate)

REYATAZ® (atazanavir sulfate) is a protease inhibitor that has been studied extensively in both treatment-naive and treatment-experienced HIV-1 infected patients and is administered once-daily in all patient populations.

Indication and Important Safety Information About REYATAZ® (atazanavir sulfate) Capsules

REYATAZ® (atazanavir sulfate) is a prescription medicine used in combination with other medicines to treat people who are infected with the human immunodeficiency virus (HIV). REYATAZ has been studied in 48-week trials in both patients who have taken or have never taken anti-HIV medicines.

REYATAZ does not cure HIV or help prevent spreading HIV to others.

REYATAZ® (atazanavir sulfate) should not be taken with the following medicines:

- Ergot medicines: ergotamine, dihydroergotamine, dihydroergotasterone.
- Nonsteroidal Anti-Inflammatory Drugs (NSAIDs): ibuprofen, naproxen, indomethacin.
- Monamine Oxidase (MAO) inhibitors: phenelzine, tranylcypromine, isocarboxazid, selegiline.
- CYP3A4 inhibitors: clarithromycin, itraconazole.
- CYP3A4 inducers: rifampin, St. John's wort.
- Certain antibiotics, antifungals, and herbal products that increase the levels of REYATAZ in the body.

People taking REYATAZ should speak with their healthcare provider before taking the following medicines:

- Anti-hypertensive: lisinopril, enalapril, captopril, quinapril, prazosin, labetalol, hydralazine.
- Male Fertility: clomiphene.
- Certain antibiotics: azithromycin, clarithromycin, erythromycin, telithromycin.
- Certain antifungals: fluconazole, itraconazole.
- Certain antidepressants: citalopram, paroxetine, venlafaxine.
- Certain medications affecting the serotonin function: sertraline, fluoxetine, paroxetine.
- Certain psychiatric medications: vitamin D, vitamin A.
- Certain hormonal treatments: hormones for male hormone therapy.

The above lists of medicines are not complete. The use of all prescriptions and non-prescription medicines, vitamins, herbal supplements, or other health preparations should be discussed with a healthcare provider.

The following side effects or conditions should be reported to a healthcare provider right away:

- A change in the way the heart beats may occur and could be a symptom of a heart problem.
- Diabetes and high blood sugar may occur in patients taking protease inhibitor medicines like REYATAZ.
- Changes in body fat have been seen in some patients taking anti-HIV medicines. The cause and long-term effects are not known at this time.
- Other side effects of REYATAZ taken with other anti-HIV medicines include: nausea, headache, stomach pain, vomiting, diarrhea, depression, fever, dizziness, trouble sleeping, numbness, and tingling or burning of hands or feet.

REYATAZ and other anti-HIV medicines should be taken exactly as instructed by your healthcare provider. United States Full Prescribing Information for REYATAZ is available at http://www.reyataz.com.

REYATAZ is a registered trademark of Bristol-Myers Squibb Company. The other brands listed are registered trademarks of their respective owners and are not trademarks of Bristol-Myers Squibb Company.

About Bristol-Myers Squibb

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