Empliciti (elotuzumab) Plus Pomalidomide and Low-Dose Dexamethasone Reduces the Risk of Disease Progression by 46% Versus Pomalidomide/Dexamethasone Alone in Patients with Relapsed or Refractory Multiple Myeloma

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Primary endpoint of progression-free survival met for the combination of Empliciti plus pomalidomide and low-dose dexamethasone

Data will be presented for the first time in late-breaking oral session during the 23rd Congress of the European Hematology Association

PRINCETON, N.J.--(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE:BMY) today announced that the ELOQUENT-3 trial, an international Phase 2 study evaluating the addition of Empliciti (elotuzumab) to pomalidomide and low-dose dexamethasone (EPd) in patients with relapsed/refractory multiple myeloma (RRMM), achieved its primary endpoint, showing a statistically significant and clinically meaningful improvement in progression-free survival (PFS) for patients treated with EPd compared with pomalidomide and dexamethasone (Pd) alone. ELOQUENT-3 is the only randomized, active-controlled trial to investigate a pomalidomide-based triplet combination in patients with RRMM who received at least two prior therapies, including lenalidomide and a proteasome inhibitor (PI).

Patients randomized to EPd experienced a 46% reduction in risk of disease progression (HR 0.54; 95% CI: 0.34 to 0.86, p=0.0078) compared with patients randomized to Pd alone, with median PFS, the study’s primary endpoint, of 10.3 months (95% CI: 5.6 to not estimable) compared with 4.7 months (95% CI: 2.8 to 7.2) in Pd patients. The PFS benefit experienced among patients randomized to EPd was consistent among patients who had received two to three prior lines of therapy (HR 0.55; 95% CI: 0.31 to 0.98) and four or more prior lines of therapy (HR 0.51; CI 95%: 0.24 to 1.08). The safety profile for EPd was consistent with prior findings for Empliciti and pomalidomide regimens. The full results will be presented in a late-breaking oral session on Sunday, June 17, at 12:30 CEST during the 23rd Congress of the European Hematology Association in Stockholm, Sweden.

“The ELOQUENT-3 trial is the first randomized trial comparing the standard of care, pomalidomide and low dose dexamethasone, with and without the addition of a monoclonal antibody. These data support the hypothesis that the addition of elotuzumab to pomalidomide and dexamethasone elicits a synergistic effect and prolongs, significantly, the progression-free survival of heavily pretreated patients with myeloma, regardless of the number of prior therapies,” said Meletios A. Dimopoulos, M.D., professor and chairman of the Department of Clinical Therapeutics at the National and Kapodistrian University of Athens, School of Medicine. “We believe that EPd, if approved by regulatory authorities, could become an important potential treatment option for patients with relapsed/refractory multiple myeloma whose disease has progressed after treatment with lenalidomide and a proteasome inhibitor.”

Twice as many patients randomized to EPd responded to therapy compared to patients randomized to Pd alone. Patients randomized to EPd demonstrated an overall response rate (ORR) of 53% (95% CI: 40 to 66), compared with 26% (95% CI: 16 to 40) among patients randomized to Pd. Time to first response was comparable for patients receiving EPd and Pd at 1.95 and 1.91 months, respectively. Median duration of response had not been reached among patients randomized to EPd at time of analysis. Overall survival, a secondary endpoint, although not mature at this time, showed a positive trend favoring EPd over Pd alone (HR 0.62; 95% CI: 0.30 to 1.28).

“Based on survival data we've seen to date in relapsed or refractory multiple myeloma, Empliciti in combination with lenalidomide and dexamethasone has been established as an important treatment option for patients,” said Jeffrey Jackson, Ph.D., hematology development lead, Bristol-Myers Squibb. “These new data evaluating the EPd combination build on our commitment to understanding the full potential of Empliciti when used in different combinations. We look forward to discussing these data with health authorities.”
Treatment-related Grade 3-4 adverse events (AEs) were comparable between EPd and Pd groups. Any-grade infections occurred in 65% of patients in both arms. Rates of the most commonly occurring Grade 3-4 hematologic AEs, neutropenia and anemia, were lower among patients receiving EPd (13% and 10%, respectively) than patients receiving Pd (27% and 20%), despite longer exposure within the EPd arm and similar dose intensity of pomalidomide between arms. AEs led to discontinuation in 18% of patients in the EPd arm, compared with 24% of patients in the Pd arm.

**About ELOQUENT-3**

The Phase 2 ELOQUENT-3 trial randomized 117 patients with RRMM who received two or more prior therapies and were either refractory or relapsed and refractory to lenalidomide and a PI. Patients were randomized 1:1 to receive either EPd (n=60) or Pd (n=57) in 28-day cycles until disease progression or unacceptable toxicity. Patients in both the EPd and Pd arms received 4 mg of pomalidomide for days 1-21 of each cycle, and the weekly equivalent of 40 mg or 20 mg dexamethasone for patients ≤75 years or >75 years, respectively. In the EPd arm, elotuzumab was administered at the dose of 10 mg/kg IV weekly for the first 2 cycles and 20 mg/kg monthly starting from cycle 3.

**Bristol-Myers Squibb & Immuno-Oncology: Advancing Oncology Research**

At Bristol-Myers Squibb, patients are at the center of everything we do. Our vision for the future of cancer care is focused on researching and developing transformational medicines, including Immuno-Oncology (I-O) therapeutic approaches, for hard-to-treat cancers that could potentially improve outcomes for these patients.

We are leading the integrated scientific understanding of both tumor cell and immune system pathways, through our extensive portfolio of investigational compounds and approved agents. Our differentiated clinical development program is studying broad patient populations across more than 50 types of cancers with 24 clinical-stage molecules designed to target different immune system pathways. Our deep expertise and innovative clinical trial designs position us to advance the I-O/I-O, I-O/chemotherapy, I-O/targeted therapies and I-O radiation therapies across multiple tumors and potentially deliver the next wave of therapies with a sense of urgency. We also continue to pioneer research that will help facilitate a deeper understanding of the role of immune biomarkers and how a patient’s tumor biology can be used as a guide for treatment decisions throughout their journey.

We understand making the promise of transformational medicines like I-O therapies a reality for the many patients who may benefit from these therapies requires not only innovation on our part but also close collaboration with leading experts in the field. Our partnerships with academia, government, advocacy and biotech companies support our collective goal of providing new treatment options to advance the standards of clinical practice.

**About Empliciti**

Empliciti is an immunostimulatory antibody that specifically targets Signaling Lymphocyte Activation Molecule Family member 7 (SLAMF7), a cell-surface glycoprotein. SLAMF7 is expressed on myeloma cells independent of cytogenetic abnormalities. SLAMF7 also is expressed on Natural Killer cells, plasma cells and at lower levels on specific immune cell subsets of differentiated cells within the hematopoietic lineage.

Empliciti has a dual mechanism-of-action. It directly activates the immune system through Natural Killer cells via the SLAMF7 pathway. Empliciti also targets SLAMF7 on myeloma cells, tagging these malignant cells for Natural Killer cell-mediated destruction via antibody-dependent cellular toxicity.

Bristol-Myers Squibb and AbbVie are co-developing Empliciti, with Bristol-Myers Squibb solely responsible for commercial activities.

**U.S. FDA-APPROVED INDICATION FOR EMPLICITI™**

EMPLICITI™ (elotuzumab) is indicated in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received one to three prior therapies.

**IMPORTANT SAFETY INFORMATION**

**Infusion Reactions**

- EMPLICITI can cause infusion reactions. Common symptoms include fever, chills, and hypotension. Bradycardia and hypertension also developed during infusions. In the trial, 5% of patients required interruption of the administration of EMPLICITI for a median of 25 minutes due to infusion reactions, and 1% of patients discontinued due to infusion reactions. Of the patients who experienced an infusion reaction, 70% (23/33) had them during the first dose. If a Grade 2 or higher infusion reaction occurs, interrupt the EMPLICITI infusion and institute appropriate medical and supportive measures. If the infusion reaction recurs, stop the EMPLICITI infusion and do not restart it on that day. Severe infusion reactions may require permanent discontinuation of EMPLICITI therapy and emergency treatment.

- Premedicate with dexamethasone, H1 Blocker, H2 Blocker, and acetaminophen prior to infusing with EMPLICITI.

**Infections**

- In a clinical trial of patients with multiple myeloma (N=635), infections were reported in 81.4% of patients in the EMPLICITI with lenalidomide/dexamethasone arm (ERd) and 74.4% in the lenalidomide/dexamethasone arm (Rd). Grade 3-4 infections were 28% (ERd) and 24.3% (Rd). Opportunistic infections were reported in 22% (ERd) and 12.9% (Rd). Fungal infections were 9.7% (ERd) and 5.4% (Rd). Herpes zoster was 13.5% (ERd) and 6.9% (Rd). Discontinuations due to infections were 3.5% (ERd) and 4.1% (Rd). Fatal infections were 2.5% (ERd) and 2.2% (Rd). Monitor patients for development of infections and treat promptly.

**Second Primary Malignancies**

- In a clinical trial of patients with multiple myeloma (N=635), invasive second primary malignancies (SPM) were 9.1% (ERd) and 7.8% (Rd). Discontinuation in 18% of patients in the EPd arm, compared with 24% of patients in the Pd arm.
and 5.7% (Rd). The rate of hematologic malignancies were the same between ERd and Rd treatment arms (1.6%). Solid tumors were reported in 3.5% (ERd) and 2.2% (Rd). Skin cancer was reported in 4.4% (ERd) and 2.8% (Rd). Monitor patients for the development of SPMs.

Hepatotoxicity

- Elevations in liver enzymes (AST/ALT greater than 3 times the upper limit, total bilirubin greater than 2 times the upper limit, and alkaline phosphatase less than 2 times the upper limit) consistent with hepatotoxicity were 2.5% (ERd) and 0.6% (Rd). Two patients experiencing hepatotoxicity discontinued treatment; however, 6 out of 8 patients had resolution and continued treatment. Monitor liver enzymes periodically. Stop EMPLICITI upon Grade 3 or higher elevation of liver enzymes. After return to baseline values, continuation of treatment may be considered.

Interference with Determination of Complete Response

- EMPLICITI is a humanized IgG kappa monoclonal antibody that can be detected on both the serum protein electrophoresis and immunofixation assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and possibly relapse from complete response in patients with IgG kappa myeloma protein.

Pregnancy/Females and Males of Reproductive Potential

- There are no studies with EMPLICITI with pregnant women to inform any drug associated risks.
- There is a risk of fetal harm, including severe life-threatening human birth defects associated with lenalidomide and it is contraindicated for use in pregnancy. Refer to the lenalidomide full prescribing information for requirements regarding contraception and the prohibitions against blood and/or sperm donation due to presence and transmission in blood and/or semen and for additional information.

Adverse Reactions

- Infusion reactions were reported in approximately 10% of patients treated with EMPLICITI with lenalidomide and dexamethasone. All reports of infusion reaction were Grade 3 or lower. Grade 3 infusion reactions occurred in 1% of patients.
- Serious adverse reactions were 65.4% (ERd) and 56.5% (Rd). The most frequent serious adverse reactions in the ERd arm compared to the Rd arm were: pneumonia (15.4%, 11%), pyrexia (6.9%, 4.7%), respiratory tract infection (3.1%, 1.3%), anemia (2.8%, 1.9%), pulmonary embolism (3.1%, 2.5%), and acute renal failure (2.5%, 1.9%).
- The most common adverse reactions in ERd and Rd, respectively (>20%) were fatigue (61.6%, 51.7%), diarrhea (46.9%, 36.0%), pyrexia (37.4%, 24.6%), constipation (35.5%, 27.1%), cough (34.3%, 18.9%), peripheral neuropathy (26.7%, 20.8%), nasopharyngitis (24.5%, 19.2%), upper respiratory tract infection (22.6%, 17.4%), decreased appetite (20.8%, 12.6%), and pneumonia (20.1%, 14.2%).

Please see the full Prescribing Information for EMPLICITI.

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 about Bristol-Myers Squibb, visit us at BMS.com or follow us on LinkedIn, Twitter, YouTube and Facebook.

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 Empliciti will receive regulatory approval for the indications described herein. 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, 2017, 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.

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$BMY presents first results from study of new potential combination in #MultipleMyeloma at #EHA23