June 12, 2015

New Post Hoc Analyses of Phase 3b Data Examine Treatment with *Orencia*® (abatacept) Plus Methotrexate (MTX) in Patients with Early Moderate to Severe Rheumatoid Arthritis (RA) and Markers of Poor Prognosis

(PRINCETON, NJ, June 9, 2015) – Bristol-Myers Squibb Company (NYSE:BMY) announced data from the Orencia® Phase 3b AVERT and AMPLE trials will be presented in three separate posters during the 2015 European League Against Rheumatism Annual Congress (EULAR 2015).

Orencia (abatacept), a biological product, is a fusion protein with novel immunosuppressive activity targeted initially at adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to certain currently available treatments. Orencia is available in both an intravenous and subcutaneous formulation in the U.S.A., Europe and Japan. In Japan, the product was approved by the Ministry of Health, Labour and Welfare to be manufactured and marketed with an indication for the treatment of rheumatoid arthritis (only for patients with an inadequate response to prior conventional therapy) on June 28, 2013

Collaboration between ONO and BMKK
ONO and BMKK concluded an agreement to jointly promote ORENCIA in September 21, 2011, and, commenced co-promotion of ORENCIA®IV on June 4, 2013. The two companies have also been co-developing ORENCIA. With ORENCIA® IV and ORENCIA® SC, we will further contribute to the treatment of rheumatoid arthritis.

Attached from the following page is the press release made by BMS for your information.

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New Post Hoc Analyses of Phase 3b Data Examine Treatment with *Orencia* (abatacept) Plus Methotrexate (MTX) in Patients with Early Moderate to Severe Rheumatoid Arthritis (RA) and Markers of Poor Prognosis

- *AVERT trial data suggests potentially faster onset of clinical response and greater drug-free clinical remission with earlier use in patients taking Orencia plus methotrexate over patients taking methotrexate alone*
- *Exploratory data of patients with high ACPA levels at baseline in the AMPLE trial suggest better response with Orencia than with adalimumab*

(PRINCETON, NJ, June 9, 2015) – Bristol-Myers Squibb Company (NYSE:BMY) announced today data from the *Orencia* Phase 3b AVERT and AMPLE trials will be presented in three separate posters during the 2015 European League Against Rheumatism Annual Congress (EULAR 2015). These trials included early moderate to severe rheumatoid arthritis (RA) patients with active disease and markers of poor prognosis, such as ACPA (anti-citrullinated protein antibody) and rheumatoid factor (RF), which are both associated with more severe disease progression and joint damage. These data suggest a correlation between ACPA and treatment outcomes, and provide further data regarding the use of *Orencia* plus methotrexate (MTX) in these RA patients. In RA, activated T-cells in the immune response drive downstream inflammatory events that produce autoantibodies. Inhibiting T-cell activation in the immune response may help reduce autoantibody formation and levels.

One post hoc analysis of AVERT (**A**ssessing **V**ery **E**arly **R**heumatoid arthritis **T**reatment) found that in patients taking *Orencia* plus MTX, the proportion of patients who maintained DAS-defined remission (DAS<2.6) following drug withdrawal was higher in patients with disease duration of three months or less (33%), compared with patients with longer disease duration (>3 to ≤6 months, 14.7%; >6 months, 10.2%). Shorter disease duration was also associated with a faster onset of clinical response.

Exploratory data from the AVERT study assessed the impact of *Orencia* plus MTX on different types of ACPA and any association with clinical response. These data suggest *Orencia* in combination with MTX had greater clinical efficacy in patients who were IgM antibody type ACPA positive at the beginning of the study than in those who were negative for that antibody type, and in those who seroconverted (changed from ACPA positive to negative) over time than those who did not (61.5% vs. 41.2% achieved Boolean remission), suggesting the impact on ACPA is associated with a clinical benefit for RA patients.

"These data are among the first to demonstrate the potential impact of a biologic therapy on ACPA in the early stages of RA, which is characterized by high autoimmune activity and the presence of autoantibodies," said T.W.J. Huizinga, M.D., PhD, Leiden University Medical Center, Leiden Netherlands. "The findings further provide insight into the role of biological response markers in helping define the disease and manage therapy."

Additionally, an exploratory analysis of AMPLE (**A**batacept Versus Adali**m**umab Com**p**arison in Bio**l**ogic-Naïv**e** rheumatoid arthritis (RA) Subjects With Background Methotrexate) suggests higher serum ACPA levels at baseline correlated with a better clinical response from *Orencia* plus MTX compared to adalimumab plus MTX. When patients were divided into quartiles based on baseline ACPA titer, significant differences in response were observed between patients in the highest titer quartile (Q4) versus Q1–3 for DAS28 (CRP) and HAQ-DI (p=0.003 and p=0.021, respectively) in the *Orencia* treated arm, while, Q4 versus Q1–3 treatment differences were not significant with adalimumab (p=0.358 and p=0.735).

"These analyses yield promising insights into RA disease progression," said Douglas Manion, M.D., Head of Specialty Development, Bristol-Myers Squibb. "With further investigation, we can provide additional understanding into the use of *Orencia* plus methotrexate in patients with early, active, moderate to severe RA."

New Analyses from the AVERT Trial

The primary results of the AVERT Phase 3b trial have been previously reported. New data being presented at EULAR 2015 include two analyses exploring the impact of earlier treatment with *Orencia* and the impact of *Orencia* on the RA disease process.

AVERT Outcomes By Baseline Disease Duration / June 12, 2015 at 12:05 PM CET: On Drug and Drug-free Remission by Baseline Disease Duration in the AVERT Trial: Abatacept versus Methotrexate Comparison in Patients with Early Rheumatoid Arthritis. VP Bykerk, et al.

The post hoc analysis examined the association of disease duration with the effects of *Orencia* plus MTX versus MTX treatment on DAS–defined remission (DAS28 [CRP] <2.6) and improvement in physical function (HAQ-DI; ≥0.3 units from baseline). The analysis included the following subgroups: 36 patients on *Orencia* plus MTX and 48 on MTX with ≤3 months disease duration; 34 patients on *Orencia* plus MTX and 29 on MTX with >3 to ≤6 months disease duration; 49 patients on *Orencia* plus MTX and 39 on MTX with >6 months disease duration. The results showed the combination of *Orencia* and MTX provided greater benefits than MTX alone in patients with a disease duration of ≤3 months: 33% of these patients maintained DAS-defined remission, compared to 14.7% of patients with a disease duration of >3 to ≤6 months and 10.2% with a duration of >6 months. Patients with ≤3 months disease duration also had the fastest onset of clinical response from *Orencia* plus MTX; as early as Day 29, 25% of patients treated with *Orencia* plus MTX with a disease duration of ≤3 months achieved DAS-defined remission, compared with 11.8% of patients with a disease duration of >3 to ≤6 months and 6.1% of patients

with a disease duration of >6 months, and 8.3% with MTX alone (≤3 month disease duration). In the MTX arm, 10.4% of patients with a disease duration of ≤3 months maintained DAS-defined remission, compared to 13.8% of patients with a disease duration of >3 to ≤6 months and 5.1% with a duration of >6 months.

AVERT ACPA – Efficacy By Baseline CCP2 Titers and Sero-Conversion Status / June 11, 2015 at 1:45 p.m. CET: Effect of Anti-Cyclic Citrullinated Peptide 2 Immunoglobulin M Serostatus on Efficacy Outcomes Following Treatment with Abatacept Plus Methotrexate in the AVERT Trial. TWJ Huizinga, et al.

This analysis explored the association between patients' ACPA and ACPA seroconversion status and efficacy outcomes of remission rate at 12 months (remission was assessed using CDAI, SDAI, Boolean, and DAS28 [CRP] <2.6-defined remission) and mean change in DAS28 (CRP) and HAQ-DI over time. A total of 200 out of the 342 patients included in the analysis were baseline anti-CCP2 IgM positive: *Orencia* plus MTX (n=66), *Orencia* monotherapy (n=62) and MTX (n=72). The results showed ACPA-IgM positive patients treated with *Orencia* plus MTX achieved the greatest mean improvements in DAS28 (CRP) and HAQ-DI over time, as well as remission in all four indices, compared with patients who were ACPA-IgM negative at baseline. In addition, 61.5% of patients in the *Orencia* plus MTX group who seroconverted (i.e., changed from ACPA-IgM positive at baseline to ACPA-IgM negative at Month 12) achieved the more stringent Boolean remission, compared to 41.2% who remained positive, suggesting an association between remission and the impact on IgM ACPA.

New Analysis from the AMPLE Trial

The primary results of the AMPLE Phase 3b trial have been previously reported. AMPLE is the first non-inferiority, head-to-head study in adults with RA comparing biologic agents, *Orencia* and adalimumab, on a background of MTX. New data being presented at EULAR 2015 includes an exploratory analysis examining outcomes in early RA patients stratified by ACPA titer.

Comparison of Patient-Reported Outcomes by Baseline ACPA Category in AMPLE / June 13, 2015 at 10:15 a.m. CET: Effect of Baseline Anti-Cyclic Citrullinated Peptide 2 Antibody Titre on Patient-Reported Outcomes Following Treatment with Subcutaneous Abatacept or Adalimumab. J Sokolove, et al.

This post hoc analysis assessed patient-reported outcomes (PROs) in 388 patients who were grouped into quartiles based on increasing ACPA titers (Q1=28-235 AU/mL; Q2=236-609 AU/mL; Q3=613-1046 AU/mL; Q4=1060-4894 AU/mL). There were 97 patients per quartile. The number of patients per treatment group in each quartile were (abatacept, adalimumab): Q1=42, 55; Q2=51, 46; Q3=46, 51; Q4=46, 51. PROs assessed included pain, quality of life, disability, and physical functioning. The results showed *Orencia* plus MTX-treated patients with the highest ACPA titers reported greater improvement than those in the lowest ACPA quartiles across measures of pain, physical function and clinical outcomes. These patterns were less pronounced among patients treated with adalimumab.

About the AVERT Trial

AVERT is a Phase 3b, active-controlled study including 351 adult patients with symptoms of moderate to severe RA for less than two years, positive for ACPA, DAS28 CRP >3.2, and naïve to treatment with MTX and biologic therapies for RA. The patients were randomly assigned to 12 months of weekly treatment in one of three groups: *Orencia* 125 mg subcutaneous plus MTX; *Orencia* 125 mg subcutaneous alone; or MTX alone. Participants who had a DAS28 CRP <3.2 (indicating low disease activity) after the 12-month treatment phase were able to continue in a withdrawal period up to 12 months, where all RA treatment including *Orencia*, MTX and steroids were withdrawn. The co-primary endpoints compared the proportion of patients with DAS28 CRP <2.6 (defined as disease remission in the trial) at month 12 and both months 12 and 18 for combination therapy versus MTX alone. Results demonstrated *Orencia* plus MTX achieved significantly higher rates of DAS-defined remission at 12 months than treatment with MTX alone (60.9% vs. 45.2%, respectively, p=0.010). Similar results at 12 months were seen with more stringent measures of efficacy including Boolean remission (37.0%, *Orencia* plus MTX; 22.4%, MTX alone), CDAI remission (42%, *Orencia* plus MTX; 27.6% MTX alone), and SDAI remission (42%, *Orencia* plus MTX; 25% MTX alone). Greater benefits on MRI endpoints were also observed with combination therapy vs. MTX alone, including improvements in synovitis and osteitis, and less progression of joint erosions. Specifically at 12 months, mean change from baseline in radiographic non-progression rates as assessed using the RAMRIS method for the synovitis score (-2.35, -1.4 and -0.68, respectively), osteitis score (-2.58, -1.36 and -0.68, respectively) and erosion score (0.19, 1.47 and 1.52, respectively) were observed for the *Orencia* with MTX, *Orencia* monotherapy and MTX groups, respectively. Serious adverse events, serious infection events and discontinuation due to serious adverse events were comparable to patients treated with MTX. Rates of serious adverse events were 6.7% and 7.8%, overall infections were 57.1% and 59.5%, serious infections were 0.8% and 0%, malignancies were 0.8% and 0.9%, and autoimmune events were 0.8% and 2.6% for the *Orencia* combination and MTX groups, respectively.

About the AMPLE Trial

AMPLE is a Phase 3b, randomized, investigator-blinded, multinational study of 24 months duration with a 12-month efficacy primary endpoint (non-inferiority for ACR20). The study included 646 adult biologic-naïve patients with active moderate to severe RA and inadequate response to MTX; 318 in the *Orencia* plus MTX group and 328 in the adalimumab plus MTX group. Patients were stratified by disease activity and randomized to either 125 mg *Orencia* SC weekly or 40 mg adalimumab every other week, both on background MTX. The primary endpoint was to determine non-inferiority of *Orencia* plus MTX to adalimumab plus MTX based on ACR20 response at 12 months. Secondary endpoints included injection site reactions, radiographic non-progression as assessed using the van der Heijde modified total Sharp score (mTSS) method, safety and retention. The complete year-one study results were published in the January 2013 volume of *Arthritis & Rheumatism*, the official monthly journal of the American College of Rheumatology. Year 2 data were consistent with Year 1. Radiographic progression was also assessed at two years with 85% of patients on the *Orencia*

regimen and 84% of patients on the adalimumab regimen achieving radiographic non-progression. At 24 months, overall safety data were similar for both groups, including frequency of adverse events (92.8% and 91.5%), serious adverse events (13.8% and 16.5%), and malignancies (2.2% and 2.1%) for the *Orencia* regimen and the adalimumab regimen, respectively.

About Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a systemic, chronic, autoimmune disease characterized by inflammation in the lining of joints (or synovium), causing joint damage with chronic pain, stiffness, and swelling. RA causes limited range of motion and decreased joint function. The condition is more common in women than in men, who account for 75% of patients diagnosed with RA.

About ORENCIA® (abatacept)

ORENCIA SC and IV is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis. ORENCIA may be used as monotherapy or concomitantly with disease-modifying antirheumatic drugs (DMARDs) other than tumor necrosis factor (TNF) antagonists.

ORENCIA IV is indicated for reducing signs and symptoms in pediatric patients 6 years of age and older with moderately to severely active polyarticular juvenile idiopathic arthritis. ORENCIA IV may be used as monotherapy or concomitantly with methotrexate (MTX). ORENCIA SC has not been studied in pediatric patients.

ORENCIA should not be administered concomitantly with TNF antagonists.

ORENCIA is not recommended for use concomitantly with other biologic rheumatoid arthritis (RA) therapy, such as anakinra.

ORENCIA is intended for use under the guidance of a physician or healthcare practitioner.

Indications/Usage and Important Safety Information for ORENCIA® (abatacept)

Indications/Usage

Adult Rheumatoid Arthritis (RA): ORENCIA® (abatacept) is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active RA. ORENCIA may be used as monotherapy or concomitantly with disease-modifying, anti-rheumatic drugs (DMARDs) other than tumor necrosis factor (TNF) antagonists.

Juvenile Idiopathic Arthritis (JIA): ORENCIA is indicated for reducing signs and symptoms in pediatric patients aged 6 years and older with moderately to severely active polyarticular JIA. ORENCIA may be used as monotherapy or concomitantly with methotrexate (MTX).

Important Limitations of Use: ORENCIA should not be administered concomitantly with TNF antagonists, and is not recommended for use concomitantly with other biologic RA therapy, such as anakinra.

Important Safety Information

Concomitant Use with TNF Antagonists: Concurrent therapy with ORENCIA® (abatacept) and a TNF antagonist is not recommended. In controlled clinical trials, adult patients receiving concomitant intravenous ORENCIA and TNF antagonist therapy experienced more infections (63%) and serious infections (4.4%) compared to patients treated with only TNF antagonists (43% and 0.8%, respectively), without an important enhancement of efficacy.

Hypersensitivity: Anaphylaxis or anaphylactoid reactions can occur during or after an infusion and can be life-threatening. There were 2 cases (<0.1%; n=2688) of anaphylaxis or anaphylactoid reactions in clinical trials with adult RA patients treated with intravenous ORENCIA. Other reactions potentially associated with drug hypersensitivity, such as hypotension, urticaria, and dyspnea, each occurred in <0.9% of patients. There was one case of a hypersensitivity reaction with ORENCIA in JIA clinical trials (0.5%; n=190). In postmarketing experience, a case of fatal anaphylaxis following the first infusion of ORENCIA was reported. Appropriate medical support measures for treating hypersensitivity reactions should be available for immediate use. If an anaphylactic or other serious allergic reaction occurs, administration of ORENCIA should be stopped immediately and permanently discontinued, with appropriate therapy instituted.

Infections: Serious infections, including sepsis and pneumonia, have been reported in patients receiving ORENCIA. Some of these infections have been fatal. Many of the serious infections have occurred in patients on concomitant immunosuppressive therapy which in addition to their underlying disease, could further predispose them to infection. Caution should be exercised in patients with a history of infection or underlying conditions which may predispose them to infections. Treatment with ORENCIA should be discontinued if a patient develops a serious infection. Patients should be screened for tuberculosis and viral hepatitis in accordance with published guidelines, and if positive, treated according to standard medical practice prior to therapy with ORENCIA.

Immunizations: Live vaccines should not be given concurrently with ORENCIA or within 3 months of its discontinuation. The efficacy of vaccination in patients receiving ORENCIA is not known. ORENCIA may blunt the effectiveness of some immunizations. It is recommended that JIA patients be brought up to date with all immunizations in agreement with current immunization guidelines prior to initiating therapy with ORENCIA.

Use in Patients with Chronic Obstructive Pulmonary Disease (COPD): Adult COPD patients treated with ORENCIA developed adverse events more frequently than those treated with placebo (97% vs 88%, respectively). Respiratory disorders occurred more frequently in patients treated with ORENCIA compared to those on placebo (43% vs 24%, respectively), including COPD exacerbations, cough, rhonchi, and dyspnea. A greater percentage of patients treated with ORENCIA® (abatacept) developed a serious adverse event compared to those on placebo (27% vs 6%), including COPD exacerbation [3 of 37 patients (8%)] and pneumonia [1 of 37 patients (3%)]. Use of ORENCIA in patients with RA and COPD should be undertaken with caution, and such patients monitored for worsening of their respiratory status.

Blood Glucose Testing: ORENCIA for intravenous administration contains maltose, which may result in falsely elevated blood glucose readings on the day of infusion when using blood glucose monitors with test strips utilizing glucose dehydrogenase pyrroloquinoline quinone (GDH-PQQ). Consider using monitors and advising patients to use monitors that do not react with maltose, such as those based on glucose dehydrogenase nicotine adenine dinucleotide (GDH-NAD), glucose oxidase, or glucose hexokinase test methods. ORENCIA for subcutaneous (SC) administration does not contain maltose; therefore, patients do not need to alter their glucose monitoring.

Pregnant and Nursing Mothers: ORENCIA should be used during pregnancy only if clearly needed. The risk for development of autoimmune diseases in humans exposed in utero to abatacept has not been determined. Nursing mothers should be informed of the risk/benefit of continued breast-feeding or discontinuation of the drug. A pregnancy registry has been established to monitor fetal outcomes. Healthcare professionals are encouraged to register pregnant patients exposed to ORENCIA by calling 1-877-311-8972.

Most Serious Adverse Reactions: Serious infections (3% ORENCIA vs 1.9% placebo) and malignancies (1.3% ORENCIA vs 1.1% placebo).

Malignancies: The overall frequency of malignancies was similar between adult patients treated with ORENCIA or placebo. However, more cases of lung cancer were observed in patients treated with ORENCIA (0.2%) than those on placebo (0%). A higher rate of lymphoma was seen compared to the general population; however, patients with RA, particularly those with highly active disease, are at a higher risk for the development of lymphoma. The potential role of ORENCIA in the development of malignancies in humans is unknown.

Most Frequent Adverse Events (≥10%): Headache, upper respiratory tract infection, nasopharyngitis, and nausea were the most commonly reported adverse events in the adult RA clinical studies. Other events reported in ≥5% of JIA patients were diarrhea, cough, pyrexia, and abdominal pain. In general, the adverse events in pediatric patients were similar in frequency and type to those seen in adult patients.

Note concerning SC ORENCIA® (abatacept): The safety and efficacy of SC ORENCIA have not been studied in patients under 18 years of age.

Please see Full Prescribing Information at http://packageinserts.bms.com/pi/pi_orencia.pdf.

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 www.bms.com, or follow us on Twitter at http://twitter.com/bmsnews

ORENCIA® **(abatacept)** is a registered trademark of Bristol-Myers Squibb Company.

About Bristol-Myers Squibb Immunoscience

The immune system is the body's natural defense against disease. These processes come into play in almost every human disease. That is why Bristol-Myers Squibb is focused on exploring ways to harness the body's own immune system to treat immune-related diseases with high unmet medical needs, including RA – a chronic, systemic, inflammatory autoimmune disorder that affects the joints.

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. 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, 2014 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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