New Head-to-Head Patient Reported Outcomes Data for Orencia® SC (abatacept) vs. Humira® (adalimumab) Presented at the 2012 American College of Rheumatology Annual Scientific Meeting

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- **Orencia SC Similar to Humira in Demonstrating Clinical Improvements in Patient Reported Outcomes in Adults with Moderate to Severe Rheumatoid Arthritis**
- **Data are from a one-year analysis of AMPLE, the first head-to-head study in adults with rheumatoid arthritis comparing Orencia SC to Humira each on a background of methotrexate**

PRINCETON, N.J.--(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE: BMY) today announced new clinical trial results showing the subcutaneous (SC) formulation of Orencia® (abatacept) on a background of methotrexate (MTX) was similar to Humira® (adalimumab) plus MTX in demonstrating clinical improvements in Patient Reported Outcomes (PROs) in adults with moderate to severe rheumatoid arthritis (RA), including patient pain, patient global assessment, fatigue, physical function and health related quality of life (HRQoL) that were sustained for one year.

At one year, Orencia SC plus MTX was similar to Humira plus MTX in improving patient pain (53.0% and 39.2%), improving patient global assessment (46.1% and 41.2%) and decreasing fatigue (-23.2% and -21.4%). A normal physical function (measured by the Health Assessment Questionnaire Disability Index, HAQ-DI) was achieved by 60.4% of patients in the Orencia SC treatment group and 57.0% in the Humira treatment group, and the measure of Health Related Quality of Life (HRQoL) assessed using SF-36 was also similar between the two groups.

The data comes from analysis of one-year results from AMPLE (Abatacept Versus Adalimumab Comparison in Biologic-Naive RA Subjects With Background Methotrexate), an ongoing, investigator-blinded randomized, Phase IIIb, controlled study comparing the efficacy of Orencia SC vs. Humira on a background of MTX in adult, biologic naïve patients with moderate to severe RA. AMPLE is a two year study with a one year efficacy primary endpoint (non-inferiority for ACR20).

"The AMPLE PRO data provides important information about Orencia and Humira in combination with MTX in RA," said Roy Fleischmann, M.D., University of Texas Southwestern Medical Center, AMPLE study investigator. "By exploring patient reported outcomes, which are associated with pain, fatigue, disability and functional loss that can significantly impact a patient’s health-related quality of life, we have advanced our understanding of an important area of focus for RA patients."

**About the Study**

AMPLE included 646 adult biologic-naïve patients with active moderate to severe RA and inadequate response to MTX; 318 in the Orencia SC® (abatacept) plus MTX group and 328 in the Humira® plus MTX group. Patients were stratified by disease activity and randomized to either 125 mg Orencia SC weekly (without an IV load) or 40 mg Humira every other week, both on background MTX. The primary endpoint was to determine non-inferiority of Orencia SC plus MTX to Humira plus MTX by a difference in 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.

PROs assessed were patient pain, patient global assessment and fatigue. Physical function was evaluated with the HAQ-DI. HRQoL was assessed using the SF-36. The Routine Assessment of Patient Index Data (RAPID3), an index of three patient reported core dataset measures, was also assessed.

**Detailed Study Results**

Improvements in all PROs measured in the study were seen at six months and sustained at one year. Improvements in patient pain (mean % ± SE) at one year were 53.0% ± 6.13 in the Orencia SC treatment group, and 39.20% ± 6.20 in the
Humira treatment group (estimate of difference: 13.80% [95% CI, -2.53, 30.14]). Improvements were also demonstrated in patient global assessment at one year (46.10% ± 3.46 with Orencia SC plus MTX and 41.21% ± 3.43 with Humira plus MTX, estimate of difference: 4.89% [95% CI, -4.37, 14.15]).

At one year, the onset and proportion of patients achieving a HAQ response indicating a normal physical function (defined as a reduction in HAQ-DI score ≥0.3 units) was similar between the two treatment groups. HAQ-DI score at baseline (mean ± SD) was 1.49 ± 0.88 in the Orencia SC group and 1.45 ± 0.68 in the Humira group. Change from baseline (mean ± SE) to year 1 in HAQ-DI was -0.60 ± 0.04, and -0.59 ± 0.03, for Orencia® (abatacept) SC and Humira®, respectively. Similar reductions in fatigue observed at six months were maintained through year one in both the Orencia SC and Humira treatment groups, and exceeded the MCID (a change of -10mm) (estimated difference: -2.42 [95% CI, -6.43, 1.59]).

**About Orencia**

Orencia® SC and IV are 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 six 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.

**Important Safety Information**

**Concomitant Use with TNF antagonists:** Concurrent therapy with ORENCIA and a biologic DMARD 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:** Less than 1% of adult patients treated with ORENCIA experienced hypersensitivity reactions, including some cases of anaphylaxis or anaphylactoid reactions. Other events potentially associated with drug hypersensitivity, such as hypotension, urticaria, and dyspnea, each occurred in less than 0.9% of patients treated with ORENCIA® (abatacept) and generally occurred within 24 hours of infusion. There was 1 case of a hypersensitivity reaction with ORENCIA in JIA clinical trials (0.5%; n = 190). Appropriate medical support measures for treating hypersensitivity reactions should be available for immediate use in the event of a reaction.

**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 as it 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 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 pyrroloquinolinequinone (GDH-PQQ). Consider using monitors and advising patients to use monitors that do not react with maltose, such as those based on glucose dehydrogenase nicotinic adenine dinucleotide (GDH-NAD), glucose oxidase, or glucose hexokinase test methods. ORENCIA® (abatacept) for subcutaneous 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). In general, adverse events in pediatric and adolescent patients were similar in frequency and type to those seen in adult patients.
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.

For US Full Prescribing Information, click here.

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, swelling and fatigue. 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 Bristol-Myers Squibb

Bristol-Myers Squibb is a global biopharmaceutical company committed to discovering, developing and delivering 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.

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