Bristol-Myers Squibb Announces U.S. FDA Breakthrough Therapy Designation for ORENCIA® (abatacept) to Help Prevent Acute Graft-Versus-Host Disease, a Potentially Life-Threatening Complication After Stem Cell Transplant

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Dateline City:
PRINCETON, N.J.

PRINCETON, N.J.--(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE: BMY) today announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation for ORENCIA® (abatacept) for the prevention of moderate to severe acute graft-versus-host disease (GvHD) in hematopoietic stem cell transplants from unrelated donors. There are no approved therapies for the prevention of acute GvHD, a potentially life-threatening medical complication that can impact patients receiving such transplants for the treatment of certain genetic diseases and hematologic cancers. Stem cell transplants have been shown to be an effective treatment for aggressive leukemias and other hematological malignancies, often representing the only therapeutic option for cure. However, some of their benefit is offset by the occurrence of severe acute GvHD, which impacts up to 40 percent of patients receiving stem cell transplants from unrelated donors with a mismatch in genes called human leukocyte antigens (HLA). These transplants are associated with a high rate of transplant-related mortality stemming largely from severe acute GvHD.

“While ideally we prefer using fully matched transplants from a sibling for the treatment of hematologic cancers, only the minority of patients have such a sibling,” said study lead investigator Leslie Kean, M.D., Director of the Stem Cell Transplantation Program, Dana Farber/Boston Children's Cancer and Blood Disorders Center. “A therapy that lowers the risk of GvHD in unrelated stem cell transplants would potentially allow more patients to receive a transplant, which typically is the last option to treat hematologic cancers after other therapies have been used unsuccessfully.”

Stem cell transplant infusions include donor T-cells, a type of white blood cell that recognizes and destroys foreign invaders in the recipient’s body including cancer cells. GvHD occurs when the donor T-cells also recognize the patient’s healthy cells as foreign and start attacking healthy tissues and organs. T-cell activation requires a signaling process called co-stimulation. ORENCIA, a therapy currently approved to treat various arthritic conditions, binds to and inhibits protein targets involved in co-stimulation, thus inhibiting T-cell activation.

The Breakthrough Therapy Designation is based on findings from an investigator-initiated study supported by Bristol-Myers Squibb. This Phase 2 trial assessed the impact of ORENCIA on the prevention of severe acute GvHD, when added to a standard GvHD prophylactic regimen administered to patients with hematologic malignancies receiving a stem cell transplant from an unrelated, HLA-matched or mismatched donor. A mismatch in HLA increases the risk of GvHD.

Breakthrough Therapy Designation is an FDA program intended to expedite the development and review of medicines for serious or life-threatening diseases with preliminary clinical evidence that the investigational therapy may offer substantial improvement on at least one clinically significant endpoint over available therapy.

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About Acute Graft-versus-Host Disease

GvHD after a hematopoietic stem cell transplant occurs when transplanted donor T-cells recognize antigenic differences between the donor and the recipient and attack the recipient’s healthy tissue and organs. Acute GvHD impacts up to 40 percent of patients who receive stem cell transplants from unrelated and HLA-mismatched donors. This activation of T-
cells can result in severe immune-mediated tissue damage to the host, with the skin, liver and gastrointestinal tract being the most common targets. Acute GvHD-mediated damage to these vital organs has been associated with increased morbidity and death.¹

About ORENCIA

ORENCIA® is an immunomodulator that disrupts the continuous cycle of T-cell activation that characterizes Rheumatoid Arthritis.

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

Indication and 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® (abatacept) is indicated for reducing signs and symptoms in patients 2 years of age and older with moderately to severely active polyarticular JIA. ORENCIA may be used as monotherapy or concomitantly with methotrexate (MTX).

Adult Psoriatic Arthritis (PsA): ORENCIA® (abatacept) is indicated for the treatment of adult patients with active PsA.

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 for ORENCIA® (abatacept)

Concomitant Use with TNF Antagonists: Concurrent therapy with ORENCIA and a TNF antagonist is not recommended. In controlled clinical trials, adult RA 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, including COPD exacerbations, cough, rhonchi, and dyspnea. In adult RA studies, 97% of COPD patients treated with ORENCIA developed adverse reactions versus 88% treated with placebo and respiratory disorders occurred more frequently in patients treated with ORENCIA compared to those on placebo (43% vs 24%, respectively), including COPD exacerbation, cough, rhonchi, and dyspnea. A greater percentage of adult RA 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 pyruvovopinoline 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 nicotinicadine 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.

Pregnancy: There are no adequate and well-controlled studies of ORENCIA use in pregnant women and the data with ORENCIA use in pregnant women are insufficient to inform on drug-associated risk. A pregnancy registry has been established to monitor pregnancy outcomes in women exposed to ORENCIA during pregnancy. Healthcare professionals are encouraged to register patients by calling 1-877-311-8972.
Lactation: There is no information regarding the presence of abatacept in human milk, the effects on the breastfed infant, or the effects on milk production. However, abatacept was present in the milk of lactating rats dosed with abatacept.

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 RA patients treated with ORENCIA or placebo. However, more cases of lung cancer were observed in RA 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 JIA and adult PsA patients were similar in frequency and type to those seen in adult RA patients.

Note concerning ORENCIA administration options: Intravenous dosing has not been studied in patients younger than 6 years of age. The safety and efficacy of ORENCIA ClickJect™ Autoinjector for subcutaneous injection has not been studied in patients under 18 years of age.

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

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

About Bristol-Myers Squibb Immunology

With a robust pipeline of immunomodulatory therapies, Bristol-Myers Squibb is committed to the discovery and development of transformational medicines that could lead to long-term remission in patients with immune-mediated diseases. As we discover more about the immune system in such diseases with substantial unmet medical needs, the potential for developing novel therapies and biomarkers of response that target specific pathways in the immune system continues to drive our research efforts.

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, Facebook and Instagram.

Cautionary Statement Regarding Forward-Looking Statements

This press release contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995 regarding, among other things, the research, development and commercialization of pharmaceutical products. All statements that are not statements of historical facts are, or may be deemed to be, forward-looking statements. Such forward-looking statements are based on historical performance and current expectations and projections about our future financial results, goals, plans and objectives and involve inherent risks, assumptions and uncertainties, including internal or external factors that could delay, divert or change any of them in the next several years, that are difficult to predict, may be outside our control and could cause our future financial results, goals, plans and objectives to differ materially from those expressed in, or implied by, the statements. These risks, assumptions, uncertainties and other factors include, among others, that future study results will be consistent with the results to date, that ORENCIA may not achieve its primary study endpoints or receive regulatory approval for the additional indication described in this release in the currently anticipated timeline or at all and, if approved, whether such product candidate for such additional indication described in this release will be commercially successful. No forward-looking statement can be guaranteed. It should also be noted that Breakthrough Therapy Designation does not change the standards for FDA approval. Forward-looking statements in this press release should be evaluated together with the many risks and uncertainties that affect Bristol-Myers Squibb’s business and market, particularly those identified in the cautionary statement and risk factors discussion in Bristol-Myers Squibb’s Annual Report on Form 10-K for the year ended December 31, 2018, as updated by our subsequent Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other filings with the Securities and Exchange Commission. The forward-looking statements included in this document are made only as of the date of this document and except as otherwise required by applicable law, Bristol-Myers Squibb undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events, changed circumstances or otherwise.

References

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