



## New SIMPONI(TM) Data Show Inhibition of Joint Damage in Patients With Rheumatoid Arthritis and Psoriatic Arthritis

### Results from Radiographic Analyses Show Efficacy of SIMPONI in Inhibiting Joint Destruction in Two Rheumatic Conditions

PHILADELPHIA, Oct 19, 2009 /PRNewswire via COMTEX News Network/ -- Phase 3 data reported for the first time show that once every four week subcutaneous injections of SIMPONI(TM) (golimumab) resulted in significantly greater inhibition of structural damage compared with placebo plus methotrexate in patients with active rheumatoid arthritis (RA) and active psoriatic arthritis (PsA). Radiographic analyses showed that treatment with SIMPONI resulted in a statistically significant reduction in change from baseline in structural damage as measured using the van der Heijde-Sharp (vdH-S) scoring method, an X-ray measure of changes in joint destruction, including joint erosion and joint space narrowing. These one-year data were presented at the 2009 American College of Rheumatology Annual Scientific Meeting.

"These findings show that treatment with golimumab and methotrexate inhibited the progression of joint damage in patients with active rheumatoid arthritis and psoriatic arthritis," said Dr. Paul Emery, head of the Academic Unit of Musculoskeletal Medicine at the University of Leeds and lead study investigator. "These data reveal important new insights into the efficacy of golimumab and its effect in altering the potential destructive nature of RA and PsA."

#### *Rheumatoid Arthritis*

At week 52 of the *G*olimumab *B*efore *E*mploying methotrexate as the *F*irst-line Option in the treatment of *R*heumatoid arthritis of *E*arly onset (*GO-BEFORE*) trial, patients with RA receiving SIMPONI plus methotrexate had significantly less progression of structural damage compared with patients receiving placebo plus methotrexate, as measured using the vdH-S score. With this method, higher scores indicate greater structural damage while lower scores indicate less structural damage. The mean change (+/- standard deviation) from baseline in patients treated with SIMPONI 50 mg plus methotrexate was a 0.74 (+/- 5.23) score compared with an increase of 1.37 (+/- 4.56) score in the group receiving placebo plus methotrexate ( $P < 0.015$ ). The reduction in progression of vdH-S scores seen with the 50 mg and 100 mg doses was comparable.

In a second study, the *G*olimumab *F*OR subjects *W*ith *A*ctive *R*A *D*espite Methotrexate (*GO-FORWARD*) clinical trial, vdH-S changes from baseline were minimal in all groups studied (including the placebo arm) which prevented any significant effect of SIMPONI to be detected. A lack of progression in the placebo group may have been due to the short placebo-controlled period of the trial and relatively less active patient population than in previously reported RA trials.

#### *Psoriatic Arthritis*

In the *G*olimumab - *A* Randomized *E*valuation of *S*afety and *E*fficacy in Subjects with *P*soriatic *A*rthritis Using a *H*uman *A*nti-TNF *M*onoclonal *A*ntibody (*GO-REVEAL*) trial, patients with active PsA receiving SIMPONI 50 mg showed significantly less progression of structural damage at week 24 compared with patients receiving placebo plus methotrexate, and the benefit was maintained through 52 weeks. Structural damage was measured using the vdH-S score. The mean change (+/- standard deviation) from baseline in patients receiving SIMPONI was a decrease of 0.16 (+/- 1.31) score at week 24 compared with an increase of 0.27 (+/- 1.26) score in the placebo group ( $P = 0.011$ ). At week 24 all placebo patients began receiving SIMPONI 50 mg. At week 52, the mean change from baseline in total vdH-S score was -0.22 (+/- 1.64) in patients initially randomized to SIMPONI 50 mg at baseline while the mean score in the group who crossed over from placebo to SIMPONI at week 24 was 0.22 (+/- 1.38).

"Results from the *GO-REVEAL* study show that treatment with golimumab inhibited joint destruction in patients with active psoriatic arthritis," said Dr. Arthur Kavanaugh, Professor of Medicine at the University of California San Diego's Division of Rheumatology, Allergy and Immunology and lead study investigator. "These findings are important as they offer new information about the efficacy of golimumab in the treatment of this complex disease."

Joint erosion (when inflammation causes bones to wear away at the joint) and joint space narrowing (when the gap between bones closes), were also measured in the study. In patients reporting no erosion at baseline, 87 percent receiving SIMPONI 50 mg remained erosion free at week 24 compared with 72 percent of patients in the placebo group ( $P = 0.003$ ). For patients reporting no joint space narrowing at baseline, 97 percent receiving SIMPONI 50 mg remained free of joint space narrowing at week 24 compared with 88 percent in the placebo group ( $P = 0.008$ ).

In April 2009, the U.S. Food and Drug Administration (FDA) and Health Canada approved SIMPONI 50 mg as a once-monthly

subcutaneous injection for the treatment of moderately to severely active RA, active PsA and active ankylosing spondylitis. In October 2009, the European Commission approved SIMPONI as a once-monthly, subcutaneous injection for the treatment of moderate to severe, active RA, active and progressive PsA and severe, active ankylosing spondylitis.

#### *About GO-BEFORE*

GO-BEFORE, a Phase 3, multi-center, double-blind, placebo-controlled study included 637 methotrexate-naive adults with RA and was designed to compare ACR 50 response at week 24 in patients receiving SIMPONI plus methotrexate compared with patients receiving placebo plus methotrexate. Patients with active RA who had more than four tender and swollen joints were included in the multicenter study. Patients were randomly assigned into four groups; Group 1 included patients receiving placebo every four weeks plus methotrexate 20 mg per week; Group 2 included patients receiving golimumab 100 mg every four weeks plus placebo every week; Group 3 and Group 4 included patients receiving SIMPONI 50 mg every four weeks plus methotrexate 20 mg per week and SIMPONI 100 mg every four weeks plus methotrexate 20 mg per week, respectively.

Adverse events were relatively similar across the four patient groups. Through week 24, serious infections were reported in two, one, one and four percent of Groups 1-4, respectively. Serious adverse events were reported in seven percent, three percent, six percent and six percent of patients in Groups 1-4, respectively.

At week 52, four patients had reported malignancies; two patients developed breast cancer, one patient developed Hodgkin's disease and one patient was diagnosed with squamous cell carcinoma of the lip. One patient developed bone tuberculosis at week 52. Two patients had died by week 52; one patient died as a result of post-surgery cardiac arrest and another patient committed suicide.

#### *About GO-FORWARD*

GO-FORWARD, a Phase 3, multi-center clinical trial included 444 patients with active RA. Adult patients with more than four tender and swollen joints, despite methotrexate therapy, were randomly assigned to receive SIMPONI (50 or 100 mg) plus methotrexate, SIMPONI 100 mg plus placebo or placebo plus methotrexate at weeks 0, 4, 8, 12, 16 and 20. Data were assessed at weeks 14 and 24. The co-primary endpoints were percentage of patients achieving ACR 20 response at week 14 and improvement from baseline in HAQ at week 24.

Through week 24, 68 percent of patients in both the combined SIMPONI plus methotrexate groups and the placebo plus methotrexate group experienced at least one adverse event. Nine percent of patients in the combined SIMPONI plus methotrexate groups experienced a serious adverse event compared with four percent of patients receiving placebo plus methotrexate. Three percent of patients in the combined SIMPONI plus methotrexate groups and one percent in the group receiving placebo plus methotrexate experienced serious infections. Rates of injection site reactions were five percent in the combined SIMPONI plus methotrexate groups and three percent in the group receiving placebo plus methotrexate.

At week 52, 11 percent of patients receiving placebo plus methotrexate reported serious adverse events compared with 17 percent of patients receiving SIMPONI 100 mg plus placebo, 14 percent of patients receiving SIMPONI 50 mg plus methotrexate and 18 percent of patients receiving SIMPONI 100 mg plus methotrexate. Two percent of patients receiving placebo plus methotrexate reported serious infections at week 52 compared with 17 percent of patients receiving SIMPONI 100 mg plus placebo, 14 percent of patients receiving SIMPONI 50 mg plus methotrexate and 18 percent of patients receiving SIMPONI 100 mg plus methotrexate. Four patients participating in the study, two receiving SIMPONI 50 mg plus methotrexate and two receiving SIMPONI 100 mg plus methotrexate, developed malignancies at week 52; two patients developed breast cancer, one patient developed squamous cell and basal cell skin cancer and one patient was diagnosed with basal cell cancer. One patient receiving SIMPONI 100 mg plus placebo died from diarrhea, colitis and sepsis.

#### *About the GO-REVEAL Trial*

The GO-REVEAL trial involved 405 adults with PsA. Patients with at least three swollen and tender joints and active psoriatic skin lesions of at least two cm in diameter were randomly assigned to receive subcutaneous injections of placebo or SIMPONI (50 or 100 mg) every four weeks for two years. The primary endpoint was ACR 20 response at week 14 for combined SIMPONI groups and individual SIMPONI dose groups vs. placebo. At week 16, patients with inadequate arthritis response were switched to SIMPONI 50 mg (patients originally receiving placebo) or SIMPONI 100 mg (patients originally receiving SIMPONI 50 mg). All patients received SIMPONI from week 24. The trial was unblinded to investigators and patients after all patients reached week 52 and the week 52 database was locked. Investigators could choose to dose escalate patients receiving SIMPONI 50 mg to 100 mg based on clinical judgment. The primary endpoint was ACR 20 response at week 14 for combined SIMPONI groups and individual SIMPONI dose groups vs. placebo.

Through week 24, the placebo-controlled portion of the study, two percent of SIMPONI-treated patients experienced serious adverse events compared with six percent of patients in the placebo group. Injection site reactions occurred in five percent of patients receiving SIMPONI and three percent of patients receiving placebo.

At week 52, four malignancies were reported; one colon, one small-cell lung cancer and two cases of basal cell carcinoma. The small-cell lung cancer patient died; another patient died in a climbing accident. Also, one patient developed liver histoplasmosis. Through one year, an analysis comparing malignancies in the study with those in a Surveillance, Epidemiology and End Results (SEER) database suggested no difference between observed and expected cases.

#### *About Rheumatoid Arthritis and Psoriatic Arthritis*

Rheumatoid arthritis is characterized by persistent and progressive joint inflammation, causing pain, stiffness and functional disability. The Arthritis Foundation estimates that approximately 1.3 million people in the United States are affected by RA. For more information, visit the [Arthritis Foundation](#).

Psoriatic arthritis is a chronic inflammatory disease that causes joint pain and swelling and can lead to joint destruction. PsA is frequently associated with inflamed, scaly, red patches of skin psoriasis and nail psoriasis. According to the National Psoriasis Foundation, up to 30 percent of people with psoriasis also develop psoriatic arthritis. For additional information visit the [National Psoriasis Foundation](#).

#### *About SIMPONI*

SIMPONI is a human monoclonal antibody that targets and neutralizes excess TNF-alpha, a protein that when overproduced in the body due to chronic inflammatory diseases can cause inflammation and damage to bones, cartilage and tissue. The first once-monthly subcutaneous anti-TNF-alpha therapy, SIMPONI is approved for the treatment of RA, PsA and ankylosing spondylitis in the United States, Europe and Canada, and is available either through the SIMPONI SmartJect autoinjector or a prefilled syringe. For more information about SIMPONI, visit [www.SIMPONI.com](http://www.SIMPONI.com).

Centocor Ortho Biotech Inc. developed and discovered SIMPONI and has exclusive marketing rights to the product in the United States. Following regulatory approvals, Schering-Plough will assume exclusive marketing rights outside the United States except in Japan, Indonesia and Taiwan, where SIMPONI will be co-marketed by Mitsubishi Tanabe Pharma Corporation and Janssen Pharmaceutical Kabushiki Kaisha; Hong Kong, where SIMPONI will be exclusively marketed by Janssen-Cilag; and China, where SIMPONI will be exclusively marketed by Xian-Janssen. Centocor Ortho Biotech, Janssen-Cilag and Xian-Janssen are wholly owned subsidiaries of Johnson & Johnson.

#### *Important Safety Information*

*SIMPONI(TM) is a prescription medicine. SIMPONI(TM) can lower your ability to fight infections. There are reports of serious infections caused by bacteria, fungi, or viruses that have spread throughout the body, including tuberculosis (TB) and histoplasmosis. Some of these infections have been fatal. Your doctor will test you for TB before starting SIMPONI(TM) and will monitor you for signs of TB during treatment. Tell your doctor if you have been in close contact with people with TB. Tell your doctor if you have been in a region (such as the Ohio and Mississippi River Valleys and the Southwest) where certain fungal infections like histoplasmosis or coccidioidomycosis are common.*

You should not start SIMPONI(TM) if you have any kind of infection. Tell your doctor if you are prone to or have a history of infections or have diabetes, HIV or a weak immune system. You should also tell your doctor if you are currently being treated for an infection or if you have or develop any signs of an infection such as:

- fever, sweat, or chills
- muscle aches
- cough
- shortness of breath
- blood in phlegm
- weight loss warm, red, or painful skin or sores on your body
- diarrhea or stomach pain
- burning when you urinate or urinate more than normal
  
- feel very tired

Tell your doctor about all the medications you take including ORENCIA (abatacept), KINERET (anakinra), RITUXAN (rituximab) or another TNF blocker, or if you are scheduled to or recently received a vaccine. People taking SIMPONI(TM) should not receive live vaccines.

Reactivation of hepatitis B virus has been reported in patients who are carriers of this virus and are taking TNF-blocker medicines, such as SIMPONI(TM). Some of these cases have been fatal. Your doctor may do blood tests before and after you

start treatment with SIMPONI(TM). Tell your doctor if you know or think you may be a carrier of hepatitis B virus or if you experience signs of hepatitis B infection, such as:

- feel very tired
- skin or eyes look yellow
- little or no appetite
- vomiting
- muscle aches
- dark urine
- clay-colored bowel movements
- fevers
- chills
- stomach discomfort
  
- skin rash

If you take SIMPONI(TM) or other TNF blockers, your risk for developing lymphoma or other cancers may increase. You should tell your doctor if you have had or develop lymphoma or other cancers.

Heart failure can occur or get worse in people who use TNF blockers like SIMPONI(TM). Your doctor will closely monitor you if you have heart failure. Tell your doctor right away if you get new or worsening symptoms of heart failure like shortness of breath or swelling of your lower legs or feet.

Rarely, people using TNF blockers can have nervous system problems such as multiple sclerosis. Tell your doctor right away if you have symptoms like vision changes, weakness in your arms or legs, or numbness or tingling in any part of your body.

Liver problems can happen in people using TNF blockers. Contact your doctor immediately if you develop symptoms such as feeling very tired, skin or eyes look yellow, poor appetite or vomiting, or pain on the right side of your stomach.

Low blood counts have been seen with people using TNF blockers. If this occurs, your body may not make enough blood cells to help fight infections or help stop bleeding. Your doctor will check your blood counts before and during treatment. Tell your doctor if you have signs such as fever, bruising, bleeding easily, or paleness.

Rarely, people using TNF blockers have developed lupus-like symptoms. Tell your doctor if you have any symptoms such as a rash on your cheeks or other parts of the body, sensitivity to the sun, new joint or muscle pain, becoming very tired, chest pain or shortness of breath, swelling of the feet, ankles, and/or legs.

New or worse psoriasis symptoms may occur. Symptoms include: red scaly patches or raised bumps that are filled with pus on the skin. These symptoms may go away or get better after stopping SIMPONI(TM).

Tell your doctor if you are allergic to rubber or latex. The needle cover contains dry natural rubber.

Tell your doctor if you have any symptoms of an allergic reaction while taking SIMPONI(TM) such as hives, swollen face, breathing trouble, chest pain.

Common side effects of SIMPONI(TM) include: upper respiratory tract infection, nausea, abnormal liver tests, redness at site of injection, high blood pressure, bronchitis, dizziness, sinus infection, flu, runny nose, fever, cold sores, numbness, or tingling.

*Please read the Medication Guide for SIMPONI(TM) and discuss any questions you have with your doctor.*

*You are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch), or call 1-800-FDA-1088.*

*About Centocor Ortho Biotech Inc.*

Centocor Ortho Biotech Inc. redefines the standard of care in immunology, nephrology, and oncology. The company was created when Ortho Biotech Inc. merged into Centocor, Inc., and Centocor, Inc. was renamed Centocor Ortho Biotech Inc. Built upon a pioneering history, Centocor Ortho Biotech Inc. harnesses innovations in large-molecule and small-molecule research to create important new therapeutic options. Beyond its innovative medicines, Centocor Ortho Biotech is at the forefront of developing education and public policy initiatives to ensure patients and their families, caregivers, advocates, and healthcare professionals have access to the latest treatment information, support services, and quality care. For more information about

Centocor Ortho Biotech, visit [www.CentocorOrthoBiotech.com](http://www.CentocorOrthoBiotech.com). Centocor Ortho Biotech is a wholly owned subsidiary of Johnson & Johnson.

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#### *About Schering-Plough*

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