



New One-Year Data from REMICADE(R) SONIC Trial Show Sustained Efficacy Compared with Azathioprine in Treatment of Crohn's Disease

--First-of-its-Kind Study Demonstrates REMICADE More Likely to Maintain Steroid-Free Remission in Patients Naive to Immunomodulators and Biologic Therapy

CHICAGO, June 2, 2009 /PRNewswire via COMTEX News Network/ -- New long-term findings from the Phase 3b study of patients with moderately to severely active Crohn's disease having inadequate response to conventional therapies, but naive to immunomodulators and biologic therapy, were presented at Digestive Disease Week today. Data from the SONIC study showed that a greater proportion of patients receiving REMICADE (infliximab) maintained steroid-free remission at one year, compared with patients receiving azathioprine alone.

"The new, year-long data reinforce earlier 26 week findings from the SONIC trial and support the importance of this first-of-its-kind study for treating Crohn's disease," said Dr. Jean-Frederic Colombel, Professor of Hepatogastroenterology, Centre Hospitalier Universitaire Lille, France, study investigator. "The data further support the use of REMICADE earlier in the treatment of moderate to severe Crohn's disease and its effectiveness in patients maintaining steroid-free remission through one year."

The SONIC clinical trial is the first of its kind to compare REMICADE, an anti-tumor necrosis factor (TNF)-alpha therapy, with an immunomodulator (azathioprine) in patients with moderate to severe Crohn's disease. Azathioprine is not approved by the U.S. Food and Drug Administration (FDA) for the treatment of Crohn's disease; however, it is widely used by gastroenterologists and other physicians in the United States to treat patients with Crohn's disease. Azathioprine is approved for the treatment of Crohn's disease in some countries outside the United States.

Patients participating in the SONIC study through 30 weeks were given the option of continuing in a blinded study extension through 54 weeks. The proportion of patients achieving steroid-free remission among the overall randomized population (N=508), including individuals who did not enter the study extension and were assumed to be non-responders to therapy or not in steroid-free remission at week 50, was 46 percent of patients receiving REMICADE and azathioprine combination therapy, and 35 percent of patients receiving REMICADE monotherapy, compared with 24 percent of patients receiving azathioprine alone (P < 0.001 REMICADE with azathioprine vs. azathioprine monotherapy; P = 0.028 REMICADE monotherapy vs. azathioprine monotherapy; P = 0.035 REMICADE with azathioprine vs. REMICADE monotherapy). In an analysis of only those individuals participating in the extension (N=280), 72 percent of patients receiving REMICADE and azathioprine combination therapy, 61 percent of patients receiving REMICADE monotherapy and 55 percent receiving azathioprine alone achieved steroid-free remission at week 50 (P = 0.010 REMICADE and azathioprine vs. azathioprine monotherapy; P = 0.324 REMICADE monotherapy vs. azathioprine monotherapy; P = 0.065 REMICADE and azathioprine vs. REMICADE monotherapy).

A final safety evaluation for those patients who entered the extension study occurred at week 54. The proportion of patients with 1 or more serious adverse events during the study was 27 percent (n=43) in the AZA monotherapy treatment group, 24 percent (n=39) in the REMICADE monotherapy treatment group, and 15 percent (n=27) in the combined REMICADE and AZA treatment group. No new serious adverse events, such as opportunistic infections, malignancies or death, were reported between weeks 30 and 54.

Dr. William J. Sandborn, Inflammatory Bowel Disease Clinic, Mayo Clinic, and principal investigator for the SONIC trial, will present the results of the SONIC extension trial on Tuesday, June 2 at 3:30 PM at the annual Digestive Disease Week meeting.

In 1998, REMICADE became the first anti-TNF-alpha therapy approved by the FDA for the treatment of moderately to severely active Crohn's disease for the reduction of the signs and symptoms in patients who have an inadequate response to conventional therapy. During the past decade, REMICADE has also become the first and only anti-TNF-alpha therapy approved by the FDA for the treatment of moderately to severely active ulcerative colitis, in patients with an inadequate response to conventional therapy, a related inflammatory bowel disease. REMICADE is also approved for the treatment of pediatric patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapies.

The SONIC study was supported by Centocor Ortho Biotech, Inc.

About SONIC

SONIC was a multicenter, Phase 3b, randomized, double-blind, controlled clinical trial designed to compare the efficacy and

safety of REMICADE monotherapy, azathioprine monotherapy and combination therapy with the 2 drugs in patients with moderately to severely active Crohn's disease who were naive to immunomodulator and biologic therapy. A total of 508 patients from the U.S., Europe and Israel were enrolled in the study and were randomized into three groups; 170 patients received azathioprine less than or equal to 2.5 mg/kg/day and placebo infusions, 169 patients received REMICADE 5 mg/kg infusions at weeks 0, 2, 6 and every 8 weeks thereafter with placebo capsules and 169 patients received REMICADE 5 mg/kg and azathioprine less than or equal to 2.5 mg/kg/day at week 26. The primary endpoint of SONIC was to assess the induction of steroid-free remission at week 26. Patients completing treatment through week 30, and who, in the opinion of the investigator, may benefit from continued treatment, entered into the study extension beginning at week 30 through week 50.

SONIC previously demonstrated the effect of REMICADE therapy on steroid-free remission and complete mucosal healing, the healing of the lining of the bowel, at week 26. Results from the 26 week data showed that 57 percent of patients receiving REMICADE combination therapy and 44 percent receiving REMICADE monotherapy achieved clinical remission without steroids compared with 31 percent of patients receiving azathioprine alone ($P < 0.001$ REMICADE with azathioprine vs. azathioprine monotherapy; $P = 0.009$ REMICADE monotherapy vs. azathioprine monotherapy; $P = 0.022$ REMICADE with azathioprine vs. REMICADE monotherapy). Additionally, mucosal healing was achieved in 44 percent of patients receiving REMICADE combination therapy and 30 percent receiving REMICADE monotherapy achieved mucosal healing compared with 17 percent of patients receiving azathioprine alone ($P < 0.001$ REMICADE with azathioprine vs. azathioprine monotherapy; $P = 0.023$ REMICADE monotherapy vs. azathioprine monotherapy; $P = 0.055$ REMICADE with azathioprine vs. REMICADE monotherapy).

Through the first 26 weeks in SONIC, 24 percent of patients receiving azathioprine monotherapy experienced one or more serious adverse events compared with 16 and 14 percent of patients receiving REMICADE monotherapy and REMICADE with azathioprine, respectively. Two patients receiving azathioprine monotherapy developed colon cancer, one patient receiving azathioprine monotherapy died following a colectomy and one patient receiving REMICADE combination therapy was diagnosed with tuberculosis. Serious infections were reported as follows: 8 in the azathioprine monotherapy group, 4 in the REMICADE monotherapy group and 6 in the REMICADE combination therapy group. There were no deaths, malignancies or reports of tuberculosis during the study extension.

For more information regarding the safety profile for REMICADE, please see "Important Safety Information" below.

About Crohn's Disease

Crohn's disease, a chronic inflammatory disease of the gastrointestinal tract, affects approximately 500,000 Americans, including approximately 150,000 pediatric patients. The cause of Crohn's disease is not known, but the disease is associated with abnormalities of the immune system that could be triggered by a genetic predisposition or diet and other environmental factors. Symptoms of Crohn's disease can vary but often include abdominal pain and tenderness, frequent diarrhea, rectal bleeding, weight loss and fever. There is currently no cure for Crohn's disease.

About REMICADE

REMICADE was the first anti-TNF-alpha treatment to be approved in three different therapeutic areas: gastroenterology, rheumatology and dermatology. REMICADE has demonstrated broad clinical utility with indications in Crohn's disease (CD), rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), ulcerative colitis (UC), pediatric Crohn's disease (PCD) and psoriasis (PsO). The safety and efficacy of REMICADE have been well established in clinical trials over the past 16 years and through commercial experience with more than one million patients treated worldwide.

In the U.S., REMICADE is approved for the following indications:

- Reducing signs and symptoms, inhibiting the progression of structural damage and improving physical function in patients with moderately to severely active RA, when administered in combination with methotrexate.
- Reducing signs and symptoms in patients with active AS.
- Reducing signs and symptoms and inducing and maintaining clinical remission in adult and pediatric patients with moderately to severely active CD who have had an inadequate response to conventional therapy.
- Reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing CD.
- Reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in patients with moderately to severely active UC who have had an inadequate response to conventional therapy.
- Reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage and improving physical function in

patients with PsA.

- Treatment of adult patients with chronic severe plaque PsO who are candidates for systemic therapy and when other systemic therapies are medically less appropriate.

REMICADE is unique among available anti-TNF biologic therapies. It is the only anti-TNF biologic administered directly by caregivers in the clinic or office setting. REMICADE is a two-hour infusion administered every 6 or 8 weeks (indication-dependent), following a standard induction regimen that requires treatment at weeks 0, 2 and 6. As a result, REMICADE patients may require as few as six treatments each year.

Important Safety Information

Only a doctor can recommend a course of treatment after checking a patient's health condition. A doctor should discuss any potential benefits and risks and help make the best treatment decision on a patient by patient basis. Like other medicines that affect the immune system, REMICADE can cause serious side effects such as lowering a patient's ability to fight infections. There are reports of serious infections caused by viruses, fungi or bacteria that have spread throughout the body, including tuberculosis (TB) and histoplasmosis. Some of these infections have been fatal. Doctors should monitor closely for signs and symptoms of TB during treatment with REMICADE. Patients should discuss any concerns about their health and medical care with their doctor.

Patients should let their doctors know if they have or ever had any of the following:

- Tuberculosis (TB) or have been near someone who has TB. Doctors will check for TB with a skin test. If a patient has latent (inactive) TB, TB treatment should begin before starting REMICADE.
- Lived in a region where certain fungal infections like histoplasmosis or coccidioidomycosis are common.
- An infection that keeps coming back (or any problems that increase the risk of infection) or have diabetes.
- Any type of cancer or a risk factor for developing cancer, for example, chronic obstructive pulmonary disease (COPD) or had phototherapy for psoriasis.
- Heart failure or any heart condition. Many people with heart failure should not take REMICADE.
- Hepatitis B virus (HBV) infection or think you may be a carrier of HBV.
- Nervous system disorders (like multiple sclerosis or Guillain-Barre syndrome).

Patients should tell their doctors about any medications they are taking, including vaccines or Kineret (anakinra), and if a woman is pregnant, plans to become pregnant or is nursing. Adults and children should not receive a live vaccine while taking REMICADE.

The following serious (sometimes fatal) side effects have been reported in people taking REMICADE.

Patients should tell their doctors right away if you have any of the signs listed below:

- Infections (like TB, blood infections, pneumonia) - fever, tiredness, cough, flu, or warm, red or painful skin or any open sores. REMICADE(R) can make patients more likely to get an infection or make any current infection worse.
- Lymphoma, or any other cancers. A rare form of fatal lymphoma has occurred mostly in teenage or young adult males with Crohn's disease or ulcerative colitis who were taking REMICADE and azathioprine or 6-mercaptopurine.
- Heart failure - new or worsening symptoms, such as shortness of breath, swelling of ankles or feet, or sudden weight gain.
- Reactivation of HBV - feeling unwell, poor appetite, tiredness, fever, skin rash and/or joint pain.
- Liver injury - jaundice (yellow skin and eyes), dark brown urine, right-sided abdominal pain, fever, or severe tiredness.

- Blood disorders - fever that doesn't go away, bruising, bleeding or severe paleness.
- Nervous system disorders - numbness, weakness, tingling, changes in your vision or seizures.
- Allergic reactions during or after the infusion - hives, difficulty breathing, chest pain, high or low blood pressure, swelling of face and hands, and fever or chills.

- Lupus-like syndrome - chest discomfort or pain that does not go away, shortness of breath, joint pain, rash on the cheeks or arms that gets worse in the sun. The more common side effects with REMICADE are respiratory infections (that may include sinus infections and sore throat), headache, rash, coughing and stomach pain.

Please read important information about REMICADE, including full U.S. prescribing information and Medication Guide, at www.remicade.com.

About Centocor Ortho Biotech Inc.

Centocor Ortho Biotech Inc. redefines the standard of care in immunology, nephrology and oncology. The company was formed when Centocor, Inc. and Ortho Biotech Inc. were consolidated in late 2008, and 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.

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