Brodalumab Treatment Improved Clinical Signs And Symptoms In Phase 2 Psoriatic Arthritis Study Published In The New England Journal Of Medicine

June 11, 2014

Phase 3 Program Underway to Further Assess Brodalumab as Potential Treatment for People Living With Psoriatic Arthritis

THOUSAND OAKS, Calif. and LONDON, June 11, 2014 /PRNewswire/ -- Amgen (NASDAQ:AMGN) and AstraZeneca today announced that results from a Phase 2 study evaluating brodalumab in 168 patients with psoriatic arthritis were published in *The New England Journal of Medicine* (NEJM). These data will also be presented at the 2014 European League Against Rheumatism (EULAR) Annual Congress in Paris on June 14, 2014 (10:15 a.m. CEST, Abstract No. SAT0404). Brodalumab is the only investigational treatment in development that binds to the interleukin-17 (IL-17) receptor and inhibits inflammatory signaling by blocking the binding of several IL-17 ligands to the receptor. The IL-17 pathway plays a central role in inducing and promoting inflammatory disease processes.

The study showed that treatment with brodalumab significantly improved signs and clinical symptoms associated with the disease, including tender and swollen joints, at 12 weeks as measured by a 20 percent improvement in the American College of Rheumatology response criteria (ACR20). The study also showed that many patients continued to improve, and that the improvements were sustained, through the first 52 weeks of the study reported in NEJM.

"Given our understanding of the role of the IL-17 receptor, we have developed a robust clinical program for brodalumab across the spectrum of inflammatory disease, including psoriasis, psoriatic arthritis and asthma," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "These encouraging psoriatic arthritis data showing that patients not only experienced improvements in clinical symptoms at week 12, but that those improvements continued over time and were sustained, were the basis for our decision to continue development of this molecule as a potential treatment for the many people who are looking to better control their disease."

The study achieved its primary endpoint with both doses of brodalumab exhibiting superiority to placebo in ACR20 responses at week 12. These responses continued to improve through 24 weeks and were sustained through the first 52 weeks of the study.[1] ACR response criteria are a measure of improvement in tender and swollen joints, as well as patient and physician global assessments of disease activity, pain, disability and inflammatory markers. A 20 percent improvement from baseline in ACR response rates is known as ACR20, a 50 percent improvement from baseline is known as ACR50 and a 70 percent improvement from baseline is known as ACR70.

"We're encouraged that treatment with brodalumab significantly reduced clinical signs and joint symptoms, compared to placebo, and that similar degrees of disease improvement were seen in biologic-treated and biologic-naive patients with psoriatic arthritis," stated Philip Mease, M.D., lead investigator and study author, Swedish Medical Center and University of Washington. "These results add to the growing body of evidence indicating that the IL-17 receptor is a promising target for the treatment of inflammatory diseases, including psoriatic arthritis."

Overall, adverse events were similar across groups with 3 percent of brodalumab-treated patients experiencing serious adverse events versus 2 percent of placebo recipients (four patients in total). Serious adverse events included skin infection (cellulitis, two cases), abdominal pain and inflammation of the gallbladder (cholecystitis). No clinically significant neutropenia ($\geq$Grade 2) was reported in this study.

"There is a significant need for new treatment options for people living with psoriatic arthritis for whom currently available treatments do not work. As an antibody targeting the IL-17 receptor, brodalumab is designed to work differently from existing treatment options," said Briggs W. Morrison, M.D., executive vice president of Global Medicines Development at AstraZeneca. "We are encouraged by the efficacy and safety profile demonstrated in this study and are investigating the potential of brodalumab in Phase 3 trials for psoriatic arthritis."

Amgen and AstraZeneca have initiated two Phase 3 studies of brodalumab in psoriatic arthritis, AMVISION-1 and AMVISION-2, which together will provide detailed information on the impact of brodalumab on improving clinical signs and symptoms in psoriatic arthritis, as well as its ability to prevent joint damage.

Study Design
The study was a Phase 2, randomized, double-blind, placebo-controlled trial designed to assess the efficacy and safety of brodalumab in psoriatic arthritis. Patients with active psoriatic arthritis were randomized to receive brodalumab (140 or 280 mg subcutaneously) or placebo at day 1 and weeks 1, 2, 4, 6, 8, and 10. At week 12, patients were offered open-label brodalumab 280 mg every two weeks.

Active psoriatic arthritis was defined by the Classification of Psoriatic Arthritis criteria (CASPAR)[2] with $\geq$3 tender and $\geq$3 swollen joints.

Detailed Results
At 12 weeks, 37 percent of patients treated with 140 mg of brodalumab (n=21/57) and 39 percent of patients treated with 280 mg of brodalumab (n=22/56) achieved an ACR20 response compared to 18 percent of patients treated with placebo (n=10/55) (p=0.03 and p=0.02, respectively).

After 12 weeks of treatment, all patients began receiving 280 mg of brodalumab every two weeks in an unblinded fashion. Improvements observed among brodalumab-treated patients in the first 12 weeks continued. At 24 weeks, 51 percent of patients treated in the first 12 weeks with 140 mg of brodalumab (n=24/47) and 64 percent of patients treated in the first 12 weeks with 280 mg of brodalumab (n=29/45) achieved ACR20 responses, compared to 44 percent of patients who switched from placebo to 280 mg of brodalumab at week 12 (n=20/46). Responses were sustained through 52 weeks.

At 12 weeks, 14 percent of patients in both groups treated with brodalumab [140 mg dose (n=8/57) and 280 mg dose (n=8/56)] achieved ACR50 responses compared to 4 percent of patients treated with placebo (n=2/55) (p=0.05 for 280 mg dose vs placebo). ACR70 responses were not significantly higher in brodalumab groups than placebo groups. At 24 weeks, 33 percent of patients in both groups initially treated with brodalumab for the first 12 weeks [140 mg dose (n=16/49) and 280 mg dose (n=15/45)], followed by 280 mg of brodalumab from weeks 12 to 24, achieved ACR50

responses compared to 20 percent of patients initially treated with placebo (n=9/46). ACR50 and ACR70 response rates continued to improve through the remainder of the study.

Safety endpoints included adverse events, which were overall similar across groups. Those most commonly reported in the combined brodalumab groups were upper respiratory tract infection (12 percent vs 7 percent for placebo), fatigue (7 percent vs 4 percent for placebo), diarrhea (6 percent vs 4 percent for placebo), and headache (6 percent vs 7 percent for placebo).

About Psoriatic Arthritis
Psoriatic arthritis is a chronic disease of the immune system that causes joint pain, stiffness and swelling that can become progressively worse over time. It may also include red patches of skin topped with silvery scales.[3] The progressive, irreversible joint damage, pain and swelling coupled with painful, scaly, red skin patches can disrupt a person's ability to perform daily activities, such as using their hands, standing for long periods or walking.[4] Psoriatic arthritis affects 30 to 50 percent[5] of approximately 125 million people worldwide who have psoriasis.[6]

About Brodalumab (AMG 827)
Brodalumab is a novel human monoclonal antibody that binds to the interleukin-17 (IL-17) receptor and inhibits inflammatory signaling by blocking the binding of several IL-17 ligands to the receptor. By stopping IL-17 ligands from activating the receptor, brodalumab prevents the body from receiving signals that may lead to inflammation. The IL-17 pathway plays a central role in inducing and promoting inflammatory disease processes. In addition to psoriatic arthritis (Phase 3), brodalumab is currently being investigated for the treatment of moderate-to-severe plaque psoriasis (Phase 3) and asthma (Phase 2).

About the Amgen and AstraZeneca Collaboration
In April 2012, Amgen and AstraZeneca formed a collaboration to jointly develop and commercialize five monoclonal antibodies from Amgen's clinical inflammation portfolio. With oversight from joint governing bodies, Amgen leads clinical development and commercialization for brodalumab (Phase 3 for moderate-to-severe plaque psoriasis and psoriatic arthritis, Phase 2 for asthma) and AMG 557/MEDI5872 (Phase 1b for autoimmune diseases such as systemic lupus erythematosus). AstraZeneca, through its biologics arm MedImmune, leads clinical development and commercialization for MEDI7183/AMG 181 (Phase 2 for ulcerative colitis and Crohn's disease), MEDI2070/AMG 139 (Phase 2 for Crohn's disease) and MEDI9929/AMG 157 (Phase 2 for asthma).

About Amgen
Amgen is committed to unlocking the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing and delivering innovative human therapeutics. This approach begins by using tools, like advanced human genetics, to unravel the complexities of disease and understand the fundamentals of human biology.

Amgen focuses on areas of high unmet medical need and leverages its biologics manufacturing expertise to strive for solutions that improve health outcomes and dramatically improve people's lives. A biotechnology pioneer since 1980, Amgen has grown to be the world's largest independent biotechnology company, has reached millions of patients around the world and is developing a pipeline of medicines with breakaway potential.

For more information, visit www.amgen.com and follow us on www.twitter.com/amgen.

About AstraZeneca
AstraZeneca is a global, innovation-driven biopharmaceutical business that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of cardiovascular, metabolic, respiratory, inflammation, autoimmune, oncology, infection and neuroscience diseases. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information please visit: www.astrazeneca.com.

Forward-Looking Statements
This news release contains forward-looking statements that are based on the current expectations and beliefs of Amgen Inc. and its subsidiaries (Amgen) and are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially from those described. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission (SEC) reports filed by Amgen Inc., including Amgen Inc.'s most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and Form 8-K. Please refer to Amgen Inc.'s most recent Forms 10-K, 10-Q and 8-K for additional information on the uncertainties and risk factors related to Amgen's business. Unless otherwise noted, Amgen is providing this information as of June 11, 2014, and expressly disclaims any duty to update information contained in this news release.

No forward-looking statement can be guaranteed and actual results may differ materially from those Amgen projects. Discovery or identification of new product candidates or development of new indications for existing products cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate or development of a new indication for an existing product will be successful and become a commercial product. Further, preclinical results do not guarantee safe and effective performance of product candidates in humans. The complexity of the human body cannot be perfectly, or sometimes, even adequately modeled by computer or cell culture systems or animal models. The length of time that it takes for Amgen and its partners to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and Amgen expects similar variability in the future. Amgen develops product candidates internally and through licensing collaborations, partnerships and joint ventures. Product candidates that are derived from relationships may be subject to disputes between the parties or may prove to be not as effective or as safe as Amgen may have believed at the time of entering into such relationship. Also, Amgen or others could identify safety, side effects or manufacturing problems with Amgen's products after they are on the market. Amgen's business may be impacted by government investigations, litigation and product liability claims. If Amgen fails to meet the compliance obligations in the corporate integrity agreement between Amgen and the U.S. government, Amgen could become subject to significant sanctions. Amgen depends on third parties for a significant portion of its manufacturing capacity for the supply of certain of its current and future products and limits on supply may constrain sales of certain of its current products and product candidate development.

In addition, sales of Amgen's products (including products of Amgen's wholly-owned subsidiaries) are affected by the reimbursement policies imposed by third-party payers, including governments, private insurance plans and managed care providers and may be affected by regulatory, clinical and

guideline developments and domestic and international trends toward managed care and healthcare cost containment as well as U.S. legislation affecting pharmaceutical pricing and reimbursement. Government and others' regulations and reimbursement policies may affect the development, usage and pricing of Amgen's products. In addition, Amgen competes with other companies with respect to some of its marketed products as well as for the discovery and development of new products. Amgen believes that some of its newer products, product candidates or new indications for existing products, may face competition when and as they are approved and marketed. Amgen's products may compete against products that have lower prices, established reimbursement, superior performance, are easier to administer, or that are otherwise competitive with its products. In addition, while Amgen and its partners routinely obtain patents for their products and technology, the protection of Amgen's products offered by patents and patent applications may be challenged, invalidated or circumvented by its competitors and there can be no guarantee of Amgen's or its partners' ability to obtain or maintain patent protection for Amgen's products or product candidates. Amgen cannot guarantee that it will be able to produce commercially successful products or maintain the commercial success of its existing products. Amgen's stock price may be affected by actual or perceived market opportunity, competitive position, and success or failure of its products or product candidates. Further, the discovery of significant problems with a product similar to one of Amgen's products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on Amgen's business and results of operations. Amgen's efforts to integrate the operations of companies it has acquired may not be successful.

The scientific information discussed in this news release relating to our product candidates is preliminary and investigative. Such product candidates are not approved by the U.S. Food and Drug Administration (FDA), and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidates.

CONTACT: Amgen, Thousand Oaks
Kristen Davis, 805-447-3008 (media)
Arvind Sood, 805-447-1060 (investors)

[1] Mease PJ, Genovese MC, Greenwald MW, et al. Brodalumab, an Anti-IL17RA Monoclonal Antibody, in Psoriatic Arthritis. *New Engl J Med*. 2014;370:2295-2306.

[2] Taylor W, Gladman D, Helliwell P, et al. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. Arthritis Rheum 2006;54(8):2665-73.

[3] Krueger G. Clinical features of psoriatic arthritis. *Am J Manag Care*. 2002;8:160-170.

[4] Krueger G, Koo J, Lebwohl M, et al. The impact of psoriasis on quality of life: results of a 1998 National Psoriasis Faproductoundation patient-membership survey. *Arch Dermatol*. 2001;137:280-4.

[5] International Federation of Psoriasis Associations. Important Facts About Psoriasis. http://www.ifpa-pso.org/web/page.aspx?refid=47. Accessed March 11, 2014.

[6] National Psoriasis Foundation. Statistics. http://www.psoriasis.org/learn_statistics. Accessed March 11, 2014.

Logo - http://photos.prnewswire.com/prnh/20081015/AMGENLOGO

SOURCE Amgen