Amgen And AstraZeneca Announce Positive Results From Third And Final Pivotal Phase 3 Study Of Brodalumab In Patients With Moderate-To-Severe Plaque Psoriasis

November 25, 2014

Study Met All Primary Endpoints Against Stelara® (ustekinumab) and Placebo
Three Pivotal Studies Form the Basis for Global Regulatory Filings, Planned In 2015

THOUSAND OAKS, Calif. and LONDON, Nov. 25, 2014 /PRNewswire/ -- Amgen (NASDAQ: AMGN) and AstraZeneca (NYSE: AZN) today announced that AMAGINE-2™, a pivotal, multi-arm Phase 3 trial evaluating two doses of brodalumab in more than 1,800 patients with moderate-to-severe plaque psoriasis, met its primary endpoints when compared with both Stelara® (ustekinumab) and placebo at week 12. Brodalumab 210 mg given every two weeks and the brodalumab weight-based analysis group were each shown to be superior to Stelara on the primary endpoint of achieving total clearance of skin disease, as measured by the Psoriasis Area Severity Index (PASI 100). When compared with placebo, a significantly greater proportion of patients treated with brodalumab achieved at least a 75 percent improvement from baseline in disease severity at week 12, as measured by the Psoriasis Area Severity Index (PASI 75). A significantly greater proportion of patients treated with brodalumab also achieved clear or almost clear skin at week 12 compared with placebo, according to the static Physician Global Assessment (sPGA 0 or 1).

Results showed that 44.4 percent of patients in the brodalumab 210 mg group, 33.6 percent of patients in the brodalumab weight-based group, 25.7 percent of patients in the brodalumab 140 mg group, 21.7 percent of patients in the Stelara group and 0.6 percent of patients in the placebo group achieved total clearance of skin disease (PASI 100). In addition, 86.3 percent of patients in the brodalumab 210 mg group, 77.0 percent of patients in the brodalumab weight-based group, 66.6 percent of patients in the brodalumab 140 mg group, 70.0 percent of patients in the Stelara group and 8.1 percent of patients in the placebo group achieved PASI 75.

"Results from AMAGINE-2 underscore that treatment with brodalumab could help a significant number of moderate-to-severe plaque psoriasis patients achieve total clearance of their skin disease, and the great majority achieve at least a 75 percent improvement in their disease," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "AMAGINE-2 is the third and final pivotal study in our Phase 3 psoriasis program and the robust data from these studies will form the basis of our global filing plan. We look forward to discussions with regulatory authorities."

All key secondary endpoints comparing brodalumab with placebo were met. The first key secondary endpoint comparing PASI 100 for brodalumab (140 mg) with Stelara at week 12 was numerically greater but not statistically significant (p=0.078). The remaining secondary endpoints against Stelara were also numerically greater (all nominal p-values were less than 0.05), but could not be deemed statistically significant due to the sequential testing method.

The most common adverse events that occurred in the brodalumab groups (more than 5 percent of patients in either group) were common cold, upper respiratory tract infection, headache and joint pain. Serious adverse events occurred in 1.0 percent of patients in the 210 mg group, 1.2 percent of patients in the weight-based group, and 2.1 percent of patients in the 140 mg group compared with 1.3 percent for Stelara and 2.6 percent for placebo during the placebo-controlled period. There was one (0.2 percent) fatal event of stroke in the brodalumab 210 mg group during the 12-week placebo-controlled induction phase, deemed by the study investigator as unrelated to treatment.

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 cytokines (A, F and A/F) to the receptor. The IL-17 receptor and cytokine family play a central role in development and clinical manifestations of plaque psoriasis.

"These results confirm our belief that targeting the IL-17 receptor to inhibit inflammatory signaling can have significant benefit for psoriasis patients," said Briggs W. Morrison, M.D., executive vice president of Global Medicines Development at AstraZeneca. "We look forward to sharing detailed results from the AMAGINE program in upcoming scientific forums."

The AMAGINE program is comprised of three pivotal Phase 3 studies designed to assess the efficacy and safety of brodalumab in patients with moderate-to-severe plaque psoriasis. Top-line results from AMAGINE-1™, comparing brodalumab with placebo, were released in May 2014. Top-line results from AMAGINE-3™, comparing brodalumab with Stelara and placebo, were announced in November 2014. AMAGINE-2 and AMAGINE-3 are identical in design.

AMAGINE-2 Study Design
AMAGINE-2 is a Phase 3 study that assessed the safety and efficacy of brodalumab given at two doses every two weeks via subcutaneous injection compared with Stelara and placebo in patients with moderate-to-severe plaque psoriasis. The study also assessed the safety and efficacy of four maintenance regimens of brodalumab. The primary endpoint comparing 210 mg of brodalumab as well as a pre-specified weight-based analysis group with Stelara was the proportion of patients achieving total clearance of skin disease, as measured by PASI 100 at week 12. When comparing brodalumab with placebo, the primary endpoints included the proportion of patients achieving at least a 75 percent improvement from baseline in disease severity (PASI 75) at week 12, and the achievement of clear or almost clear skin, according to the sPGA (0 or 1) at week 12.

The study began with a 12-week, double-blind, active comparator- and placebo-controlled induction phase, where patients were randomized in a 2:2:1:1 ratio to receive brodalumab (210 mg or 140 mg), Stelara (per the labeled dose), or placebo. At week 12, patients originally randomized to either brodalumab arm were re-randomized 2:2:2:1 into the maintenance phase to receive brodalumab 210 mg or 140 mg at four different maintenance regimens. Patients originally randomized to Stelara continued to receive the same treatment, and those originally randomized to receive placebo began 210 mg of brodalumab every two weeks.

At week 52, patients entered the long-term extension portion of the study, and those who were originally randomized to receive Stelara began receiving 210 mg of brodalumab every two weeks. All other patients continued on treatment with brodalumab at the same dose they were being treated with at week 52. Patients may be enrolled in the study for up to 271 weeks (approximately five years). Amgen will continue to collect efficacy

and safety data during this long-term exposure period.

A PASI score is a measure of psoriatic plaque redness, scaling and thickness and the extent of involvement in each region of the body. Treatment efficacy is often measured by the reduction of PASI from baseline (e.g., a 75 percent reduction is known as PASI 75, a 90 percent reduction is known as PASI 90 and PASI 100 is total clearance of skin disease).

sPGA is a physician's rating of psoriasis severity at a given point in time based on plaque, scaling and redness. A physician can rate a patient's psoriasis as clear (0), almost clear (1), mild (2), moderate (3), severe (4), or very severe (5).

About Psoriasis
Psoriasis is a serious, chronic inflammatory disease that causes raised, red, scaly patches to appear on the skin, typically affecting the outside of the elbows, knees or scalp, though it can appear on any location.[1,2] Approximately 125 million people worldwide have psoriasis and 80 percent of those patients have plaque psoriasis.[3,4]

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.[5] In addition to moderate-to-severe plaque psoriasis (Phase 3), brodalumab is currently being investigated for the treatment of psoriatic arthritis (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, we or us) 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 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 our business. Unless otherwise noted, we are providing this information as of Nov. 25, 2014, and expressly disclaim 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 we project. 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 us and our partners to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and we expect similar variability in the future. We develop 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 we may have believed at the time of entering into such relationship. Also, we or others could identify safety, side effects or manufacturing problems with our products after they are on the market. Our business may be impacted by government investigations, litigation and product liability claims. If we fail to meet the compliance obligations in the corporate integrity agreement between us and the U.S. government, we could become subject to significant sanctions. We depend on third parties for a significant portion of our manufacturing capacity for the supply of certain of our current and future products and limits on supply may constrain sales of certain of our current products and product candidate development.

In addition, sales of our products (including products of our 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 our products. In addition, we compete with other companies with respect to some of our marketed products as well as for the discovery and development of new products. We believe that some of our newer products, product candidates or new indications for existing products, may face competition when and as they are approved and marketed. Our products may compete against products that have lower prices, established reimbursement, superior performance, are easier to administer, or that are otherwise competitive with our products. In addition, while we and our partners routinely obtain patents for our and their products and technology, the protection of our products offered by patents and patent applications may be challenged, invalidated or circumvented by our or our partners' competitors and there can be no guarantee of our or our partners' ability to obtain or maintain patent protection for our products or product candidates. We cannot guarantee that we will be able to produce commercially successful products or maintain the commercial success of our existing products. Our stock price may be affected by actual or perceived market opportunity, competitive position, and success or failure of our products or product candidates. Further, the discovery of significant problems with a product similar to one of our products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on our business and results of operations. Our efforts to integrate the operations of companies we have acquired may not be successful. Cost savings initiatives may result in us incurring impairment or other related charges on our assets. We may experience difficulties, delays or unexpected costs and not achieve anticipated benefits and savings from our recently announced restructuring plans. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or our ability to pay a dividend or repurchase common stock.

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

Stelara® is a registered trademark of Janssen Biotech, Inc.

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References:

1. National Psoriasis Foundation. Symptoms and diagnosis. http://www.psoriasis.org/about-psoriasis/symptoms-and-diagnosis. Accessed on September 10, 2014.
2. National Psoriasis Foundation. Frequently Asked Questions. http://www.psoriasis.org/about-psoriasis/faqs. Last updated 2014. Accessed on September 10, 2014.
3. International Federation of Psoriasis Associations. Psoriasis is a Serious Disease Deserving Global Attention: A report by the International Federation of Psoriasis Associations. www.ifpa-pso.org/getfile.ashx?cid=279366&cc=3&refid=18. Accessed on September 10, 2014.
4. American Academy of Dermatology. Psoriasis. http://www.aad.org/media-resources/stats-and-facts/conditions/psoriasis. Last updated 2014. Accessed on September 10, 2014.
5. Miossec P, Korn T, Kuchroo VK. Interleukin-17 and Type 17 Helper T Cells. The New England Journal of Medicine. 2009; 361: 888-98.

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