# Amgen Announces Updates to the U.S. Prescribing Information for ESAs

November 8, 2007

**Revised Class Labeling Based on Data Discussed at the May 2007 ODAC and September 2007 CRDAC Meetings**

**Six Additional Studies Added to Current Pharmacovigilance Program**

THOUSAND OAKS, Calif.--(BUSINESS WIRE)--Nov. 8, 2007--Amgen (NASDAQ:AMGN) today announced that it has updated the Aranesp(R) (darbepoetin alfa) and EPOGEN(R)/PROCRIT(R) (Epoetin alfa) package inserts in collaboration with the U.S. Food and Drug Administration (FDA) and Johnson and Johnson Pharmaceutical Research & Development (J&JPRD). The changes to the labeling include modifications to the boxed warnings, additional language in the INDICATIONS AND USAGE section, addition of an oncology study to the WARNINGS section, and clarification of the hemoglobin range for chronic renal failure (CRF) patients in the DOSAGE AND ADMINISTRATION section.

The Company also announced that it has developed a comprehensive clinical study pharmacovigilance program designed to address outstanding questions about ESA safety in both investigational and labeled settings. Six new proposed clinical trials have been designed to assess the safety of erythropoiesis-stimulating agents (ESAs) when used to treat chemotherapy-induced anemia in specific tumor types. Upon FDA agreement, these studies will be added to the ongoing pharmacovigilance program, which was agreed to with the FDA after the 2004 Oncologic Drug Advisory Committee (ODAC) meeting.

"Amgen has been working closely with the FDA and J&JPRD to ensure that the information contained in the approved labeling for ESAs accurately reflects the current state of knowledge of these important products and to develop a comprehensive and feasible clinical study program to complement our existing pharmacovigilance program," said Roger M. Perlmutter, M.D., Ph.D., executive vice president of Research and Development at Amgen. "In the current label revisions, we have endeavored to include as much information as possible so physicians and their patients can make informed treatment decisions."

The Company plans to hold a conference call with the investment community at 7:00 a.m. Pacific Time on Thursday, Nov. 8, 2007, to discuss these latest developments.

ESA Label Update

The modifications to the package insert reflect ongoing interactions with the FDA regarding the safety and benefit/risk profile of ESAs. These changes recognize input from the ODAC meeting held on May 10, 2007, and the joint Cardiovascular-Renal Drug Advisory Committee (CRDAC)/Drug Safety & Risk Management Advisory Committee (DSaRMAC) meeting held on Sept. 11, 2007.

The revised boxed warning provides disease specific guidance for chronic renal failure, cancer, and perisurgery indications, including the following modifications:

- The boxed warning has additional language specific to renal failure that states: "Patients experienced greater risks for death and serious cardiovascular events when administered ESAs to target higher versus lower hemoglobin levels (13.5 vs. 11.3 g/dL; 14 vs. 10 g/dL) in two clinical studies. Individualize dosing to achieve and maintain hemoglobin levels within the range of 10 to 12 g/dL."

- The boxed warning for the cancer indication has been updated to describe studies in patients with advanced breast, head and neck, lymphoid and non-small cell lung malignancies. These studies administered ESAs to target a hemoglobin level greater than or equal to 12 g/dL and were associated with shortened overall survival and/or time to tumor progression. The warning specifically states: "The risks of shortened survival and tumor promotion have not been excluded when ESAs are dosed to target a hemoglobin of less than 12 g/dL. To minimize these risks as well as the risk of serious cardio- and thrombovascular events, use the lowest dose needed to avoid red blood cell transfusions." Physicians are further advised to use ESAs only if patients are receiving concomitant myelosuppressive chemotherapy and to discontinue ESA treatment following the completion of a chemotherapy course.

- The boxed warning for the perisurgery indication has additional language specific to perisurgery patients stating: "EPOGEN increased the rate of deep venous thromboses in patients not receiving prophylactic anticoagulation. Consider deep venous thrombosis prophylaxis." (Note perisurgery language appears only in the EPOGEN prescribing information as Aranesp is not approved for this indication).

The WARNINGS, Increased Mortality, Serious Cardiovascular and Thromboembolic Events were modified to include "Patients with chronic renal failure and an insufficient hemoglobin response to ESA therapy may be at even greater risk for cardiovascular events and mortality than other patients." The WARNINGS, Increased Mortality and/or Tumor Progression section was modified to include a table summarizing studies added to the label, including the Phase 3 study in lymphoid malignancies (161 study).

The DOSAGE AND ADMINISTRATION instructions for CRF patients were modified to individualize dosing to achieve and maintain hemoglobin levels between the range of 10 to 12 g/dL. For patients who do not attain a hemoglobin level within this range despite the use of appropriate ESA dose titration over a 12-week period, the instructions were modified to not administer higher ESA doses and to use the lowest dose that will maintain a hemoglobin level sufficient to avoid the need for recurrent red blood cell transfusions. Additional instructions include that monitoring of the hemoglobin level should be continued and discontinuation of ESAs if responsiveness does not improve and the patient needs recurrent red blood cell transfusions.

DOSAGE AND ADMINISTRATION instructions for cancer patients were modified to reinforce that ESA therapy should be discontinued following the completion of a chemotherapy course. The labeling continues to recommend that the dose should be adjusted for each patient to achieve and maintain the lowest hemoglobin level sufficient to avoid the need for red blood cell transfusion and not to exceed the upper safety limit of 12 g/dL.

The patient populations covered in the indications have not changed. However, the revised labeling reiterates that ESAs are not indicated for use in patients receiving hormonal agents, therapeutic biologic products, or radiotherapy unless receiving concomitant myelosuppressive chemotherapy. For the Aranesp product labeling the oncology indication now states that in controlled clinical trials, ESA use has not been demonstrated to improve symptoms of anemia, quality of life, fatigue, or patient well-being. The updated EPOGEN product labeling no longer contains patient-reported outcomes from older clinical studies that did not meet recent criteria for inclusion in the label based on FDA draft guidance, but does state EPOGEN use improved exercise tolerance and patient-reported physical function in dialysis patients.

Amgen submitted the changes announced today to the FDA under the regulatory mechanism known as a "changes being effected" (CBE) and these changes are effective immediately. However, discussions with the FDA are ongoing, and Amgen intends to submit further modifications to ESA product labeling to address other issues raised at the ODAC meeting. The company expects these discussions will result in additional revisions to class product labeling.

In the meantime, Amgen will advise prescribing health care professionals of the current changes in the form of a Dear Health Care Professional (DHCP) letter over the coming weeks. Prescribers are encouraged to review the full prescribing information, which will be posted on www.amgen.com, www.aranesp.com, and www.epogen.com.

Additionally, the European Medicines Agency's (EMEA) Committee for Medicinal Products for Human Use (CHMP) recently reviewed the latest clinical data for ESAs and announced that it will update the prescribing information for ESAs in the European Union. The updated labeling will stipulate a uniform target hemoglobin range for all ESAs of 10 to 12 g/dL with a warning not to exceed 12 g/dL. Both the EMEA and FDA revised labels continue to provide physician discretion to treat patients based upon their clinical judgment.

Pharmacovigilance Program Updates

Additionally, Amgen has discussed six additional study concepts with the FDA to address potential safety concerns in patients with non small-cell lung cancer (two studies) and lymphoproliferative malignancy (four studies). Based on the safety signals observed with higher hemoglobin levels, a study to evaluate the effect of hemoglobin target on the risk/benefit profile of ESAs is also planned.

The original pharmacovigilance program included both investigator-sponsored and company-sponsored studies, and became part of a formal post-marketing commitment with the FDA in 2006. All studies that Amgen has responsibility for have either been completed or are on track for completion by the commitment date.

Overall, we believe that the ongoing and planned pharmacovigilance studies will result in a robust body of well-controlled data to address concerns regarding survival and tumor progression in these patient populations, including a total of three studies in breast cancer, three studies in lung cancer (1 SCLC and 2 NSCLC), five studies in lymphoproliferative malignancy, one study in head and neck cancer, and one study to evaluate the effect of target hemoglobin levels.

Investor Call at 7:00 a.m. PT

The Company plans to hold a conference call with the investment community at 7:00 a.m. Pacific Time on Thursday, Nov. 8, 2007, to discuss these latest developments.

Live audio of the conference call will be simultaneously broadcast over the Internet and will be available to members of the news media, investors and the general public.

The webcast of the conference, as with other selected presentations regarding developments in Amgen's business given by management at certain investor and medical conferences, can be found on Amgen's Web site, www.amgen.com, under Investors. Information regarding presentation times, webcast availability, and webcast links are noted on Amgen's Investor Relations Events Calendar. The webcast will be archived and available for replay 72 hours after the event.

About Aranesp

Aranesp was approved by the U.S. Food and Drug Administration (FDA) in September 2001 for the treatment of anemia associated with CRF for patients on dialysis and patients not on dialysis. In July 2002, the FDA approved weekly dosing of Aranesp for the treatment of anemia caused by concomitantly administered chemotherapy in patients with nonmyeloid malignancies and in March 2006, the FDA approved every-three-week dosing in these patients.

About EPOGEN

Amgen launched EPOGEN, one of the first biologically derived human therapeutics, into the U.S. medical marketplace in 1989 for the treatment of anemia in patients with chronic renal failure on dialysis. EPOGEN is a recombinant protein with the same mechanism of action as endogenous human erythropoietin, a protein produced by the kidneys to stimulate the production of oxygen-transporting red blood cells.

Important Aranesp and EPOGEN Safety Information

WARNINGS: INCREASED MORTALITY, SERIOUS CARDIOVASCULAR and THROMBOEMBOLIC EVENTS, and TUMOR PROGRESSION

Renal failure: Patients experienced greater risks for death and serious cardiovascular events when administered erythropoiesis- stimulating agents (ESAs) to target higher versus lower hemoglobin levels (13.5 vs. 11.3 g/dL; 14 vs. 10 g/dL) in two clinical studies. Individualize dosing to achieve and maintain hemoglobin levels within the range of 10 to 12 g/dL.

Cancer:
- ESAs shortened overall survival and/or time-to-tumor progression in clinical studies in patients with advanced breast, head and neck, lymphoid, and non-small cell lung malignancies when dosed to target a hemoglobin of greater than or equal to 12 g/dL.

-The risks of shortened survival and tumor progression have not been excluded when ESAs are dosed to target a hemoglobin of less than 12 g/dL.

- To minimize these risks, as well as the risk of serious cardio- and thrombovascular events, use the lowest dose needed to avoid red blood cell transfusions.

-Use only for treatment of anemia due to concomitant myelosuppressive chemotherapy.

- Discontinue following the completion of a chemotherapy course. Perisurgery: EPOGEN(R) increased the rate of deep venous thromboses in patients not receiving prophylactic anticoagulation. Consider deep venous thrombosis prophylaxis.

Aranesp and EPOGEN are contraindicated in patients with uncontrolled hypertension.

About Amgen

Amgen discovers, develops and delivers innovative human therapeutics. A biotechnology pioneer since 1980, Amgen was one of the first companies to realize the new science's promise by bringing safe and effective medicines from lab, to manufacturing plant, to patient. Amgen therapeutics have changed the practice of medicine, helping millions of people around the world in the fight against cancer, kidney disease, rheumatoid arthritis and other serious illnesses. With a deep and broad pipeline of potential new medicines, Amgen remains committed to advancing science to dramatically improve people's lives. To learn more about our pioneering science and our vital medicines, visit www.amgen.com.

Forward-Looking Statements

This news release contains forward-looking statements that involve significant risks and uncertainties, including those discussed below and others that can be found in our Form 10-K for the year ended Dec. 31, 2006, and in our periodic reports on Form 10-Q and Form 8-K. Amgen is providing this information as of the date of this news release and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

No forward-looking statement can be guaranteed and actual results may differ materially from those we project. The Company's results may be affected by our ability to successfully market both new and existing products domestically and internationally, clinical and regulatory developments (domestic or foreign) involving current and future products, sales growth of recently launched products, competition from other products (domestic or foreign), difficulties or delays in manufacturing our products. In addition, sales of our products are affected by reimbursement policies imposed by third-party payors, 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 health care 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. Furthermore, our research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. 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 products liability claims. Further, while we routinely obtain patents for our products and technology, the protection offered by our patents and patent applications may be challenged, invalidated or circumvented by our competitors. 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, we compete with other companies with respect to some of our marketed products as well as for the discovery and development of new products. Discovery or identification of new product candidates cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate will be successful and become a commercial product. Further, some raw materials, medical devices and component parts for our products are supplied by sole third-party suppliers.

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