Amgen Statement on CHMP Opinion on Vectibix(R) (Panitumumab) Use With Chemotherapy in Metastatic Colorectal Cancer

March 18, 2011

THOUSAND OAKS, Calif., March 18, 2011 /PRNewswire via COMTEX/ --

Amgen (Nasdaq: AMGN) today issued the following statement:

Amgen has received notice that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a negative opinion for Amgen's application to extend the marketing authorization in Europe for Vectibix(R) (panitumumab) to include combination with chemotherapy for the treatment of patients with wild-type *KRAS* metastatic colorectal cancer (mCRC).

Amgen will review the CHMP opinion and consider appropriate next steps, as Amgen believes that Vectibix in combination with chemotherapy provides an important treatment option for patients with wild-type *KRAS* mCRC. Amgen remains committed to patients with this aggressive disease, for whom there are limited treatment options.

Vectibix is already approved and established in more than 30 countries outside of the United States (U.S.) as a monotherapy treatment for patients with wild-type *KRAS* mCRC, when standard chemotherapy is no longer effective. In the U.S., Vectibix received accelerated approval in September 2006 as a monotherapy for the treatment of patients with EGFR-expressing mCRC after disease progression on or following fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens. Furthermore, use of Vectibix is not recommended in patients whose tumors have *KRAS* mutations in codon 12 or 13. In Japan and Israel, Vectibix is approved for use in combination with chemotherapy for patients with wild-type *KRAS* mCRC.

Data from studies 20050203 (PRIME) and 20050181 ('181') showed that adding Vectibix to FOLFOX and FOLFIRI chemotherapy, respectively, improved progression-free survival (PFS) versus chemotherapy alone in patients with wild-type *KRAS* mCRC. Patients taking this combination have a greater chance of living longer without their disease getting worse. Additionally, the response rate of Vectibix plus chemotherapy was higher than chemotherapy alone. Although numerically greater, the improvement in median overall survival (OS) did not achieve statistical significance in the Vectibix arm of either trial.(i)(ii)

In general, adverse events rates were comparable across arms in both studies, with the exception of known toxicities associated with anti-EGFR therapy, such as rash, diarrhea, and hypomagnesemia. Vectibix-related grade 3/4 infusion reactions were reported in less than one percent of patients. In patients with mutated *KRAS* tumors, outcomes were inferior for those receiving Vectibix plus FOLFOX versus FOLFOX alone. (iii)(iv)

About *KRAS*

Results from studies performed over the last 25 years indicate that *KRAS* plays an important role in cell growth regulation. In mCRC, EGFR transmits signals through a set of intracellular proteins. Upon reaching the nucleus, these signals instruct the cancer cell to reproduce and metastasize, leading to cancer progression.(v) Anti-EGFR antibody therapies work by inhibiting the activation of EGFR, thereby inhibiting downstream events that lead to malignant signaling. However, in patients whose tumors harbor a mutated *KRAS* gene, the *KRAS* protein is always turned "on," regardless of whether the EGFR has been activated or therapeutically inhibited. *KRAS* mutations occur in approximately 40-50 percent of mCRC patients.(vi)(vii)

About Colorectal Cancer

Colorectal cancer is the third most common cancer worldwide in men and the second most common in women. In 2008, approximately 1.23 million cases of colorectal cancer were diagnosed globally.(viii) In 2008, there were an estimated 333,330 new cases of colorectal cancer in the EU.(ix)

About Vectibix

Vectibix is the first fully human anti-EGFR antibody approved by the U.S. Food and Drug Administration (FDA) for the treatment of mCRC. Vectibix was approved in the U.S. in September 2006 as a monotherapy for the treatment of patients with EGFR-expressing mCRC after disease progression on or following fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens.

The effectiveness of Vectibix as a single agent for the treatment of EGFR-expressing mCRC is based on progression-free survival. Currently no data are available that demonstrate an improvement in disease-related symptoms or increased survival with Vectibix.

Retrospective subset analyses of mCRC trials have not shown a treatment benefit for Vectibix in patients whose tumors had *KRAS* mutations in codon 12 or 13. Use of Vectibix is not recommended for the treatment of colorectal cancer with these mutations.(x)

In December 2007, the European Medicine Agency (EMA) granted a conditional marketing authorization for Vectibix as a monotherapy for the treatment of patients with EGFR-expressing mCRC with non-mutated (wild-type) *KRAS* after failure of fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens.(xi) Vectibix has been launched in more than 30 European Union countries, Russia, Israel, Switzerland, Australia, Canada and Japan. Applications in the rest of the world are pending.

Important European Product Safety Information

For full prescribing information please see the Summary of Product Characteristics.

Vectibix is indicated as monotherapy for the treatment of patients with EGFR-expressing, metastatic colorectal carcinoma (mCRC) with nonmutated (wild-type) *KRAS* after failure of fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens.

Vectibix is contraindicated in patients with a history of severe or life-threatening hypersensitivity reactions to the product and in patients with interstitial

pneumonitis or pulmonary fibrosis.

Other common adverse events of special importance associated with Vectibix and/or EGFR monoclonal antibody therapies include dermatologic-related reactions, pulmonary complications, electrolyte disturbances and infusion-related reactions (including rare reports with fatal outcome). These events should be monitored carefully, see Summary of Product Characteristics for information on appropriate management of these adverse events. Acute renal failure has been observed in patients who develop severe diarrhoea and dehydration.

Vectibix should not be used in combination with IFL [bolus 5-fluorouracil (500 mg/m2), leucovorin (20 mg/m2) and irinotecan (125 mg/m2)] or in combination with bevacizumab containing chemotherapy.

Vectibix should not be administered in combination with oxaliplatin-containing chemotherapy to mCRC patients with mutant *KRAS* tumours or for whom *KRAS* tumour status is unknown.

About Amgen

Amgen discovers, develops, manufactures, 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, 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, bone disease, 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 vital medicines, visit www.amgen.com.

Forward-Looking Statements

This statement contains forward-looking statements that are based on management's current expectations and beliefs 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, including Amgen's most recent annual report on Form 10-K and most recent periodic reports on Form 10- Q and Form 8-K. Please refer to Amgen'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, Amgen is providing this information as of March 18, 2011 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 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 modelled by computer or cell culture systems or animal models. The length of time that it takes for us 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 products liability claims. 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 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 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 and there can be no guarantee of our 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.

The scientific information discussed in this statement related to our product candidates is preliminary and investigative and is not part of the labeling approved by the U.S. FDA or the European Medicines Agency (EMA) for the products. The products are not approved for the investigational use(s) discussed in this news release, and no conclusions can or should be drawn regarding the safety or effectiveness of the products for these uses. Only the FDA, EMA or other applicable regulatory bodies can determine whether the products are safe and effective for these uses. Healthcare professionals should refer to and rely upon the approved labeling for the products, and not the information discussed in this statement.

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(Logo: http://photos.prnewswire.com/prnh/20081015/AMGENLOGO)

(i) Douillard, JE et al. Randomized, Phase 3 Study (PRIME) of Panitumumab with FOLFOX4 versus FOLFOX4 Alone as First-Line Treatment in Patients With Previously Untreated Metastatic Colorectal Cancer. *J Clin Oncol 28.* 2010.

(ii) Peeters, M et al. Randomized Phase III Study of Panitumumab With Fluorouracil, Leucovorin, and Irinotecan (FOLFIRI) Compared With FOLFIRI Alone As Second-Line Treatment in Patients With Metastatic Colorectal Cancer. *J Clin Oncol 28,* 2010.

(iii) Adverse event rates were comparable across arms with the exception of known toxicities associated with anti-epidermal growth factor receptor (EGFR) therapy such as rash, diarrhea and hypomagnesemia. Vectibix-related grade 3 infusion reactions were reported for two patients (less than 1 percent).

(iv) In general, adverse events rates were comparable across arms with the exception of known toxicities associated with anti-epidermal growth factor receptor (EGFR) therapy such as rash, diarrhea, and hypomagnesemia. Vectibix-related grade 3/4 infusion reactions were reported in less than one percent of patients.

(v) Malumbres, M. and Barbacid, M. *RAS* oncogenes: the first 30 years. *Nature Reviews Cancer*. 3:459-65, 2003.

(vi) Karapentis C, S. Snell, L, E. The Laboratory Assessment of KRAS Mutation Status in Colorectal Cancer.Asia, *Pacific Journal of Oncology and Hematology*. 2010.

(vii) Friday BB and Adjei AA. K-ras as a target for cancer therapy. *Biochim. Biophys. Acta* 1756: 127-144, 2005.

(viii) Ferlay J, Shin HR, Bray F, Forman D, Mathers C and Parkin DM. GLOBOCAN 2008, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10.Lyon, France: International Agency for Research on Cancer; 2010.

(ix) Ferlay J, Parkin DM, Steliarova-Foucher E Estimates of cancer incidence and mortality in Europe in 2008. Eur J Cancer. 2010 Mar; 46(4):765-81. Epub 2010 Jan 29.

(x) Vectibix (panitumumab) [prescribing information]. Thousand Oaks, Calif: Amgen; 2011.

(xi) Vectibix (panitumumab) SPC. Thousand Oaks, Calif: Amgen; 2011.

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