Two Pivotal Vectibix(R) Phase 3 Studies in First and Second-Line Treatment of Metastatic Colorectal Cancer Published in the Journal of Clinical Oncology

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Data Shows Vectibix Combined with Chemotherapy Improved Progression-Free Survival in Patients with Wild-type KRAS mCRC

THOUSAND OAKS, Calif., Oct 04, 2010 /PRNewswire via COMTEX/ --

Amgen (Nasdaq: AMGN) today announced that results from the PRIME '203' and '181' pivotal Phase 3 trials evaluating Vectibix(R) (panitumumab) in combination with chemotherapy (FOLFOX or FOLFIRI) as a first and second-line treatment for metastatic colorectal cancer (mCRC), respectively, were published online in the *Journal of Clinical Oncology*.

"Both studies demonstrated that Vectibix administered with chemotherapy significantly improved progression-free survival in patients with wild-type *KRAS* mCRC," said Marc Peeters, M.D., Ph.D., Professor of Oncology, Antwerp University Hospital and '181' trial lead investigator and study author. "The adverse event profiles in both trials were as expected for an anti-EGFR antibody treatment used in combination with these types of chemotherapy regimens. Additionally, these data reinforce that *KRAS* status should be known when choosing treatment strategies."

PRIME '203' Results in First-Line mCRC Demonstrate Vectibix Combined with Chemotherapy (FOLFOX) Helped Patients with Wild-type *KRAS* mCRC Live Longer Without their Disease Worsening (Progression-Free Survival or PFS)

- The addition of Vectibix to FOLFOX (an oxaliplatin-based chemotherapy) significantly improved PFS (median 9.6 months for Vectibix plus FOLFOX versus 8.0 months for patients treated with FOLFOX alone, hazard ratio 0.80; 95 percent CI: 0.66-0.97; p=0.02) in the first-line treatment of patients with wild-type *KRAS* mCRC.
- Although numerically greater (23.9 months versus 19.7 months, hazard ratio 0.83; 95 percent CI: 0.67-1.02), the improvement in overall survival (OS) (secondary endpoint) in the Vectibix arm did not achieve statistical significance (p=0.072) in the same patient population.
- Importantly, in patients with tumors harboring activating *KRAS* mutations, PFS was significantly inferior in the Vectibix arm. For patients with mutant *KRAS* tumors, median PFS was 7.3 months with Vectibix in combination with FOLFOX versus 8.8 months with FOLFOX alone (hazard ratio 1.29; 95 percent CI: 1.04-1.62; p=0.02).
- These data confirm previous findings when oxaliplatin-based chemotherapy and an anti-EGFR antibody were combined in patients bearing tumors with activating *KRAS* mutations.
- The response rate of Vectibix plus chemotherapy was higher than chemotherapy alone in the wild-type *KRAS* patient population as measured by blinded central review (55 percent versus 48 percent in the FOLFOX only arm).
- Tumor *KRAS* status was ascertained in 93 percent of the 1,183 patients enrolled in the PRIME '203' trial, the highest number ever prospectively reported for a first-line trial.

"The outcome of this high quality trial demonstrated that Vectibix, which was administered every two weeks, improved progression-free survival as a first-line metastatic colorectal cancer treatment in a selected patient population," said Jean Yves-Douillard, M.D., Ph.D., director Clinical and Translational Research, Medical Oncology Branch, Centre R Gauducheau, France and PRIME '203' trial lead investigator and study author.

'181' Results in Second-Line mCRC Demonstrate Vectibix Combined with Chemotherapy (FOLFIRI) Helped Patients with Wild-type *KRAS* mCRC Live Longer Without their Disease Worsening (PFS)

- Results of the '181' trial showed that the addition of Vectibix to FOLFIRI (an irinotecan-based chemotherapy) significantly improved PFS (co-primary endpoint) (median 5.9 months for Vectibix plus FOLFIRI versus 3.9 months for patients treated with FOLFIRI alone, hazard ratio 0.73; 95 percent CI: 0.59-0.90; p=0.004) in the second-line treatment of patients with wild-type *KRAS* mCRC.
- Although numerically greater (median 14.5 months versus 12.5 months; hazard ratio 0.85; 95 percent CI: 0.70-1.04), the improvement in overall survival (co-primary endpoint) in the Vectibix arm did not achieve statistical significance (p=0.12) in the same patient population.
- The addition of Vectibix to chemotherapy in the '181' trial resulted in greater than a three-fold improvement (35 percent versus 10 percent) in response rate in the wild-type *KRAS* patient population, as measured by a blinded central review.
- Tumor *KRAS* status was ascertained in 91 percent of the 1,186 patients enrolled in the '181' trial, the highest number ever prospectively reported for a second-line trial.
- In this study, the addition of Vectibix had no positive or negative effect on PFS or OS in patients with tumors harboring activating *KRAS* mutations.

"The response rate seen in the '181' trial is among the highest ever reported in the second-line metastatic colorectal cancer setting," said Emily Chan, M.D., Ph.D., Assistant Professor of Medicine, Vanderbilt-Ingram Cancer Center and '181' study investigator and author. "Additionally, the tissue acquisition from both the '181' and '203' studies has yielded a large repository of informative data regarding the *KRAS* biomarker, and holds the potential of providing even more information in the future."

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.

Originally designed to compare the treatment effect in the overall mCRC patient population, both studies were amended to analyze outcomes with respect to the presence or absence of activating mutations in *KRAS* in the tumor itself. These are the first Phase 3 studies to prospectively analyze the effect of an EGFR inhibitor based on *KRAS* status in patients with previously treated mCRC.

Results from both trials were previously presented at Europe's largest cancer conference, ECCO 15 - ESMO 34, in September 2009, at the 2010 American Society of Clinical Oncology (ASCO) Gastrointestinal Cancers Symposium in January, and at the 2010 American Society of Clinical Oncology (ASCO) Annual Meeting in June.

About the PRIME '203' Trial

Patients enrolled in the '203' or PRIME trial (Panitumumab Randomized trial In combination with chemotherapy for Metastatic colorectal cancer to determine Efficacy) were randomized to receive either 6.0 mg/kg of Vectibix and FOLFOX4 once every two weeks (Q2W) or FOLFOX4 alone Q2W. The primary endpoint of the study was progression-free survival by *KRAS* status and secondary endpoints included overall survival, objective response rate, time to progression, duration of response and safety. Long-term follow up for overall survival is ongoing.

About the '181' Trial

The '181' trial is a global, multicenter, randomized Phase 3 study. Patients enrolled in the study were randomized to receive either 6.0 mg/kg of Vectibix and FOLFIRI Q2W or FOLFIRI alone Q2W. The co-primary endpoints were progression-free survival (which was independently tested) and overall survival. Secondary endpoints included objective response rate, time to progression, duration of response and safety by *KRAS* status.

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. 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.

About Colorectal Cancer

Colorectal cancer is the fourth most common cancer in men and the third most common cancer in women worldwide. Approximately 1.2 million cases of colorectal cancer are expected to occur globally. With more than 630,000 deaths worldwide per year, it is the third leading cause of cancer-related death in the Western world. The highest incidence rates are found in Japan, North America, parts of Europe, New Zealand, and Australia, and rates are low in Africa and Southeast Asia. Rates are substantially higher in men than in women.

About Vectibix

Vectibix is the first fully human anti-EGFR antibody approved by the United States (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.

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. Vectibix has been launched in more than 20 European Union countries, Russia, Israel, Switzerland, Australia, Canada and Japan. Applications in the rest of the world are pending.

Important U.S. Product Safety Information

WARNING: DERMATOLOGIC TOXICITY and INFUSION REACTIONS

Dermatologic Toxicity: Dermatologic toxicities occurred in 89 percent of patients and were severe (NCI-CTC grade 3 or higher) in 12 percent of patients receiving Vectibix monotherapy. [See Dosage and Administration (2.1), Warnings and Precautions (5.1), and Adverse Reactions (6.1)].

Infusion Reactions: Severe infusion reactions occurred in approximately 1 percent of patients. Fatal infusion reactions occurred in postmarketing experience [See Dosage and Administration (2.1), Warnings and Precautions (5.2), and Adverse Reactions (6.1, 6.3)].

The most common adverse events of Vectibix are skin rash with variable presentations, hypomagnesemia, paronychia, fatigue, abdominal pain, nausea, and diarrhea, including diarrhea resulting in dehydration.

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 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 http://www.amgen.com.

Forward-Looking Statements

This news release 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 Oct. 4, 2010 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 modeled 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 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 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 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 (FDA), and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidates. Only the FDA can determine whether the product candidates are safe and effective for the use(s) being investigated. Further, the scientific information discussed in this news release relating to new indications for our products is preliminary and investigative and is not part of the labeling approved by the U.S. FDA 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 can determine whether the products are safe and effective for these uses. Healthcare professionals should refer to and rely upon the FDA approved labeling for the products, and not the information discussed in this news release.

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