New Analyses Identify Predictive Biomarkers For Vectibix® (Panitumumab) In Patients With Metastatic Colorectal Cancer

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Biomarker Analysis From Phase 3 PRIME ('203) Study and Phase 2 PEAK ('509) Study Link Additional RAS Gene Mutations to Vectibix Clinical Response

THOUSAND OAKS, Calif., May 15, 2013 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced results from three analyses of Vectibix® (panitumumab) in combination with FOLFOX, an oxaliplatin-based chemotherapy regimen, as a first-line treatment for metastatic colorectal cancer (mCRC). These analyses include the description of new predictive biomarkers of clinical response to Vectibix, activating mutations in *KRAS* (beyond exon 2) and mutations in *NRAS*, collectively referred to as *RAS*.

"Amgen helped establish *KRAS* gene mutation as a biomarker for lack of response to anti-EGFR treatment," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "The identification of new biomarkers may further help to identify appropriate patients with this incurable disease for such treatment."

The *RAS* biomarkers were identified in a predefined retrospective subset analysis of the PRIME trial, where *RAS* was defined as exons 2, 3 and 4 of *KRAS* and *NRAS*. Mutational status of tumors was determined by Sanger sequencing in parallel with WAVE®-based SURVEYOR® Scan Kits (CRC *RAS*can ™) from Transgenomic, Inc. (TBIO). In this exploratory analysis, patients with wild-type *RAS* mCRC who were administered Vectibix in combination with FOLFOX demonstrated an improvement in median overall survival (OS) of 26.0 months compared to 20.2 months for patients treated with FOLFOX alone (HR = 0.78, 95 percent CI, 0.62-0.99).

Patients with mutant *RAS* tumor status had inferior progression-free survival (PFS) (HR = 1.34, 95 percent CI, 1.07-1.60) and OS (HR = 1.25, 95 percent CI, 1.02-1.55) when administered Vectibix in combination with FOLFOX chemotherapy versus FOLFOX alone. These results suggest that *RAS* mutation status beyond *KRAS* may be predictive of negative outcomes in patients receiving Vectibix plus FOLFOX in mCRC. Amgen is working to inform investigators and physicians of this important new safety information, as well as working with regulatory agencies regarding appropriate communication of the outcomes of this analysis.

Results of this study will be presented at the 2013 American Society of Clinical Oncology (ASCO) Annual Meeting on Tuesday, June 4, 8:00 a.m. - 12:00 p.m. CDT, S405 (Abstract No. 3511; Poster Discussion).

In a separate and updated exploratory analysis of longer follow-up of OS of the PRIME trial (primary endpoint of PFS), an improvement in OS was observed in patients with wild-type *KRAS* exon 2 mCRC treated with Vectibix in combination with FOLFOX. Median OS was 23.8 months compared to 19.4 months for patients treated with FOLFOX alone (HR = 0.83, 95 percent CI, 0.70-0.98). In both PRIME analyses, the most commonly reported adverse events for the Vectibix treatment arms included rash, hypomagnesemia and diarrhea. The adverse event profiles for the wild-type tumor and mutant tumor populations were similar.

Updated results of the study will be presented at the 2013 ASCO Annual Meeting on Sunday, June 2, 8:00 a.m. - 11:45 a.m. CDT, S Hall A2 (Abstract No. 3620; Poster).

In a separate predefined secondary objective subset analysis of the PEAK study, patients with wild-type *RAS* mCRC treated with Vectibix in combination with FOLFOX had a median PFS of 13.1 months compared to 9.5 months (HR = 0.63, 95 percent CI, 0.43-0.94) for patients treated with bevacizumab in combination with FOLFOX. Median OS was not reached in the Vectibix arm, but the OS HR favored the Vectibix arm (HR = 0.55, 95 percent CI, 0.33-1.01). The most commonly reported adverse events for the Vectibix treatment arm included rash, hypomagnesemia and dehydration. The adverse event profiles for the wild-type tumor and mutant tumor populations were similar. No new toxicities were identified for Vectibix.

Updated results of the study will be presented at the 2013 ASCO Annual Meeting on Sunday, June 2, 8:00 a.m. - 11:45 a.m. CDT, S Hall A2 (Abstract No. 3631; Poster).

PRIME ('203) Study Design

The PRIME (Panitumumab Randomized trial In combination with chemotherapy for Metastatic colorectal cancer to determine Efficacy) ('203) trial is a global, multicenter, randomized Phase 3 study designed to evaluate (primary endpoint of PFS) Vectibix (6.0 mg/kg every two weeks) plus FOLFOX versus FOLFOX alone in patients with wild-type *KRAS* exon 2 mCRC. The primary objective of this predefined retrospective subset analysis was to determine the effect of Vectibix plus FOLFOX versus FOLFOX alone on overall survival in patients with mCRC based on *RAS* or *BRAF* mutation status. A total of 641 patients were included in this analysis. *RAS* status was ascertained in 90 percent of the patients with wild-type *KRAS* tumors.

PEAK ('509) Study Design

The PEAK (Panitumumab Efficacy in Combination with mFOLFOX6 Against bevacizumab plus mFOLFOX6 in mCRC subjects with wild-type *KRAS* tumors) ('509) trial is a global, multicenter, randomized Phase 2 study designed to compare the efficacy (primary endpoint of PFS) of Vectibix in combination with FOLFOX to the efficacy of bevacizumab in combination with FOLFOX in patients with previously untreated, unresectable, wild-type *KRAS* exon 2 mCRC. The primary objective of this predefined retrospective subset analysis was to determine the effect of Vectibix plus FOLFOX versus bevacizumab plus FOLFOX on PFS and OS in patients with mCRC based on *RAS* mutation status.

About *KRAS* and *RAS*

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.[1] 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. Common *KRAS* mutations occurring in exon 2 (codons 12/13) are present in approximately

40 to 50 percent of mCRC patients.[2,3] *RAS* mutations are mutations occurring in exons 2, 3 and 4 of *KRAS* and *NRAS* and based on study data, appear to occur in approximately 16 percent of patients with wild-type *KRAS* exon 2.

About Colorectal Cancer
Colorectal cancer is the third most common cancer found in both men and women in the United States, and is the second leading cause of cancer deaths.[4,5] Approximately 1.2 million people are living with colorectal cancer globally. 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.[6]

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 United States in September 2006 as a single agent for the treatment of patients with EGFR-expressing mCRC with 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 PFS. More than half of patients who receive Vectibix monotherapy respond to treatment with an average six month PFS benefit. 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 mCRC with these mutations.[7]

Important U.S. Product Information
Vectibix is indicated as a single agent for the treatment of EGFR-expressing mCRC with 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 demonstrate an improvement in disease-related symptoms or increased survival with Vectibix.

Vectibix is not indicated for the treatment of patients with *KRAS* mutation-positive mCRC or for whom *KRAS* mCRC status is unknown. Retrospective subset analyses of metastatic colorectal cancer trials have not shown a treatment benefit for Vectibix in patients whose tumors had *KRAS* mutations in codon 12 or 13.

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 one 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.

The most serious adverse reactions of Vectibix are pulmonary fibrosis, pulmonary embolism, severe dermatologic toxicity complicated by infectious sequelae and septic death, infusion reactions, abdominal pain, hypomagnesemia, nausea, vomiting and constipation.

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 people around the world in the fight against serious illnesses. With a deep and broad pipeline of potential new medicines, Amgen remains committed to advancing science to dramatically improve people's lives. For more information, visit www.amgen.com and follow us on www.twitter.com/amgen.

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 any subsequent 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 May 15, 2013, 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 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 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 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. Food and Drug Administration (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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(Logo: http://photos.prnewswire.com/prnh/20081015/AMGENLOGO)

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