Phase 3 Trial Comparing Vectibix® (Panitumumab) to Erbitux® (Cetuximab) Meets Primary Endpoint Of Non-Inferiority Of Overall Survival

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Trial Evaluated Nearly 1,000 Patients With Metastatic Colorectal Cancer

THOUSAND OAKS, Calif., Sept. 28, 2013 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced detailed results from the Phase 3 ASPECCT ('763) trial comparing Vectibix® (panitumumab) to Erbitux® (cetuximab) for the treatment of wild-type *KRAS* metastatic colorectal cancer in patients who have not responded to chemotherapy. The study met its primary endpoint, demonstrating that panitumumab was non-inferior to cetuximab for overall survival. The results were presented in an oral presentation at the 17th ECCO - 38th ESMO - 32nd ESTRO European Cancer Congress in Amsterdam (Abstract No. 18).

The prospective study showed that the median overall survival for patients treated with panitumumab was 10.4 months (range 9.4 months to 11.6 months) compared to 10 months (range 9.3 months to 11.0 months) for patients treated with cetuximab (95 percent CI, 0.84-1.11, *p*=0.0007).

Colorectal cancer is the second leading cause of cancer deaths.[1,2] Approximately 1.2 million cases of colorectal cancer are expected to occur globally.

"ASPECCT was a well-conducted and robust Phase 3 trial involving nearly 1,000 patients globally with metastatic colorectal cancer," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "Colorectal cancer is a devastating disease and these results provide physicians with important new information about the role Vectibix can play as they evaluate treatment options."

In the study, progression-free survival was a median of 4.1 months in patients treated with panitumumab versus 4.4 months in patients treated with cetuximab (HR=1.00, 95 percent CI, 0.88, 1.14). Objective response rate, which is the percentage of patients who experienced tumor size reduction, was 22 percent for patients treated with panitumumab compared to 19.8 percent for patients in the cetuximab arm (Odds Ratio 1.15, 95 percent CI, 0.83, 1.58).

In the safety analysis, the profiles of both treatments were consistent with previously reported studies. Adverse events (AEs) included known events such as rash, low levels of magnesium in the blood and infusion reactions.

In Europe, the ASPECCT trial is a Specific Obligation for Vectibix as part of the European Medicine Agency's (EMA) conditional marketing authorization.

ASPECCT ('763) Trial Design

ASPECCT is a global, randomized, multicenter, open-label, Phase 3 non-inferiority trial designed to compare the effect of panitumumab versus cetuximab on overall survival for monotherapy treatment of chemorefractory metastatic colorectal cancer (mCRC) in 999 patients with wild-type *KRAS* tumors (primary endpoint). Secondary endpoints included safety, patient reported outcomes, progression-free survival, time to response, time to treatment failure and duration of response.

Patients were randomized in a 1:1 ratio to receive 6 mg/kg of intravenous panitumumab every 14 days or 400 mg/m^2 of an initial dose of intravenous cetuximab, followed by 250 mg/m^2 of intravenous cetuximab every seven days.

About *KRAS*

Results from studies performed over the last 30 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.[3] 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.[4,5]

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 *RAS* mutations. In the EU, the use of Vectibix is not recommended for the treatment of colorectal cancer with these mutations.

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. Vectibix in combination with oxaliplatin-based chemotherapy is not indicated for the treatment of patients with *RAS* (*KRAS* or *NRAS*) mutation-positive mCRC or for whom *RAS* status is unknown.

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.

Important EU Product Information

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

Vectibix is indicated for the treatment of adult patients with wild-type *RAS* metastatic colorectal cancer (mCRC):

- in first-line in combination with FOLFOX.
- in second-line in combination with FOLFIRI for patients who have received first-line fluoropyrimidine-based chemotherapy (excluding irinotecan).
- as monotherapy 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.

The combination of Vectibix with oxaliplatin-containing chemotherapy is contraindicated for patients with mutant *RAS* mCRC or for whom *RAS* mCRC status is unknown.

Other adverse events of special importance associated with Vectibix and/or EGFR monoclonal antibody therapies include dermatologic-related reactions, pulmonary complications, electrolyte disturbances, infusion-related reactions (including rare reports with fatal outcome) and ocular toxicities. 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. For patients with ECOG 2 performance status, assessment of benefit-risk is recommended prior to initiation of Vectibix in combination with chemotherapy for treatment of mCRC.

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.

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.

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 Sept. 28, 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.

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

[1] Cancer Facts and Figures 2013. American Cancer Society website. http://www.cancer.org/acs/groups/content/@epidemiologysurveilance/documents/document/acspc-036845.pdf. Accessed March 25, 2013.

[2] Colorectal Cancer Prevention (PDQ®). National Cancer Institute. Accessed March 25, 2013. http://www.cancer.gov/cancertopics/pdq/prevention/colorectal/HealthProfessional/page3.

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

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

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

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