Amgen Presents New Data Supporting First-Line Use Of Vectibix® (Panitumumab) In Combination With FOLFOX In Patients With Wild-Type RAS Metastatic Colorectal Cancer

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Exploratory Analysis of Phase 2 Trial Shows Earlier and Sustained Responses in Patients Treated With Vectibix Versus Bevacizumab

Separate Analysis of Phase 3 Trial Demonstrates no Differences in Quality of Life Between FOLFOX Regimens With or Without Vectibix

THOUSAND OAKS, Calif., Jan. 15, 2015 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced new data from the Phase 2 PEAK and Phase 3 PRIME studies that support the first-line use of Vectibix® (panitumumab) in combination with FOLFOX, an oxaliplatin-based chemotherapy regimen, in patients with wild-type *RAS* (absence of exons 2, 3, or 4 *KRAS* or *NRAS* mutations) metastatic colorectal cancer (mCRC). The data will be presented during a poster session at the 2015 American Society of Clinical Oncology (ASCO) Gastrointestinal Cancers Symposium taking place in San Francisco from January 15 to 17.

In an exploratory analysis from the PEAK study (abstract #660), treatment with Vectibix compared to bevacizumab (Avastin®) resulted in a significantly higher proportion of patients with earlier tumor shrinkage at week eight (64 percent vs. 45 percent, respectively; 95 percent CI, p=0.0232), and among responding patients, a significantly longer duration of response (11.4 vs. 8.5 months, respectively; 95 percent CI, p=0.0142) and greater depth of response (65 percent vs. 46 percent, respectively; p=0.0007). Overall response rates (ORR) appeared to be similar between Vectibix and bevacizumab. This is consistent with observed overall survival (OS) and progression-free survival (PFS) rates, and with data previously reported. The safety profile of Vectibix was consistent with previously reported studies.

"These analyses help deepen our understanding of how Vectibix works when added to a standard first-line chemotherapy for the treatment of wild-type *RAS* metastatic colorectal cancer," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "Our Vectibix clinical trial program continues to yield new insights regarding biomarkers and drug sequencing."

While the primary analysis from PEAK showed similar ORR between the Vectibix- and bevacizumab-based regimens, this exploratory analysis demonstrates that Vectibix produces early, sustained anti-tumor activity, which may in part explain the OS and PFS benefits seen with Vectibix versus bevacizumab in this trial.

A separate analysis from the Phase 3 PRIME study (abstract #537), demonstrated that there were no significant differences in quality of life among patients treated with Vectibix plus FOLFOX versus FOLFOX alone despite the incidence of adverse events associated with each treatment regimen. The quality of life analysis included a scale that assessed mobility, self-care, usual activities, pain/discomfort and anxiety/depression.

Colorectal cancer is the third most common cancer found in both men and women in the U.S. and is the second leading cause of cancer deaths.[1,2] Approximately 1.2 million cases of colorectal cancer are expected to occur globally each year.[3]

About the PEAK Study

The PEAK (Panitumumab Efficacy in Combination with mFOLFOX6 Against bevacizumab plus mFOLFOX6 in mCRC subjects with wild-type *KRAS* tumors) ('509) study is a global, multicenter, randomized, interventional Phase 2 trial designed to compare efficacy of first-line Vectibix (panitumumab) in combination with mFOLFOX6 versus bevacizumab in combination with mFOLFOX6 in 285 previously untreated patients with wild-type *KRAS* exon 2 metastatic colorectal cancer (mCRC). Primary endpoints include progression-free survival (PFS), and secondary endpoints include overall survival (OS), percentage of patients with objective response (OR), duration of response (DoR), depth of response (DpR) and safety.

Patients were randomized in a 1:1 ratio to receive 6 mg/kg of intravenous panitumumab and mFOLFOX6, or 5 mg/kg of intravenous bevacizumab and mFOLFOX6 every 14 days.

In the exploratory analyses of tumor assessments, DpR was defined as the percentage of tumor shrinkage at nadir (point in time between chemotherapy cycles in which a patient experiences low blood counts) or progression. Early tumor shrinkage (ETS) was defined as the proportion of patients with ≥30 percent tumor shrinkage at week eight.

About the PRIME Study

The PRIME (Panitumumab Randomized trial In combination with chemotherapy for Metastatic colorectal cancer to determine Efficacy) ('203) study is a global, multicenter, randomized Phase 3 study designed to evaluate Vectibix (panitumumab) in combination with FOLFOX versus FOLFOX alone in 1,183 patients with wild-type *KRAS* exon 2 metastatic colorectal cancer (mCRC). Primary endpoints include progression-free survival (PFS), and secondary endpoints include overall survival (OS), objective response rate (ORR), duration of response (DoR) and safety.

Patients were randomized in a 1:1 ratio to receive 6 mg/kg of panitumumab (day 1) and FOLFOX (day 1 and 2), or FOLFOX (day 1 and 2) alone of each 14-day cycle.

In this analysis, quality of life (QoL) was assessed every four weeks until disease progression, and once at a safety follow-up, using the EuroQoL 5-domain health state index and overall health rating (OHR; 0-100 visual analogue scale).

About Vectibix® (panitumumab)

Vectibix is the first fully human anti-EGFR antibody approved by the U.S. Food and Drug Administration (FDA) for the treatment of metastatic colorectal cancer (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 after prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy.

In May 2014, the FDA approved Vectibix for use in combination with FOLFOX, as first-line treatment in patients with wild-type KRAS (exon 2) mCRC.

With this approval, Vectibix became the first- and- only biologic therapy indicated for use with FOLFOX, one of the most commonly used chemotherapy regimens, in the first-line treatment of mCRC for patients with wild-type KRAS mCRC.

Important U.S. Product Information
Vectibix is indicated for the treatment of patients with wild-type *KRAS* (exon 2 in codons 12 or 13) mCRC as determined by an FDA-approved test for this use:

- As first-line therapy in combination with FOLFOX
- As monotherapy following disease progression after prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy

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

RAS is defined as exon 2 (codons 12 and 13), exon 3 (codons 59 and 61), and exon 4 (codons 117 and 146) of either KRAS or NRAS and hereon is referred to as "RAS."

WARNING: DERMATOLOGIC TOXICITY
Dermatologic Toxicity: Dermatologic toxicities occurred in 90 percent of patients and were severe (NCI-CTC grade 3 or higher) in 15 percent of patients receiving Vectibix monotherapy. [See Dosage and Administration (2.1), Warnings and Precautions (5.1), and Adverse Reactions (6.1)]

A predefined retrospective subset analysis of a clinical study further identified a shortening of progression-free survival (PFS) and overall survival (OS) in patients with RAS-mutant tumors who received Vectibix and FOLFOX versus FOLFOX alone. Determination of RAS-mutant tumor status should be performed by an experienced laboratory.

Determination of *KRAS* mutational status in colorectal tumors using an FDA-approved test indicated for this use is necessary for selection of patients for treatment with Vectibix. Patients with *KRAS*-mutant mCRC tumors receiving Vectibix in combination with FOLFOX experienced shorter OS compared to FOLFOX alone.

Progressively decreasing serum magnesium levels leading to severe (Grade 3-4) hypomagnesemia occurred in up to 7% of patients across clinical trials. Monitor patients for hypomagnesemia and hypocalcemia prior to initiating Vectibix treatment, periodically during Vectibix treatment, and for up to 8 weeks after the completion of treatment.

In a clinical trial, 4% of patients experienced infusion reactions and 1% of patients experienced severe infusion reactions (NCI-CTC grade 3-4).

Severe diarrhea and dehydration, leading to acute renal failure and other complications, have been observed in patients treated with Vectibix in combination with chemotherapy.

Fatal and non-fatal cases of interstitial lung disease (ILD) (1%) and pulmonary fibrosis have been observed in patients treated with Vectibix. Pulmonary fibrosis occurred in less than 1% (2/1467) of patients enrolled in clinical studies of Vectibix. In the event of acute onset or worsening of pulmonary symptoms, interrupt Vectibix therapy. Discontinue Vectibix therapy if ILD is confirmed.

The most common adverse reactions of Vectibix are skin rash with variable presentations, paronychia, fatigue, nausea and diarrhea. The most frequently reported serious, adverse reactions of Vectibix are general physical health deterioration, and intestinal obstruction.

The most commonly reported adverse reactions of Vectibix in combination with FOLFOX are diarrhea, stomatitis, mucosal inflammation, asthenia, paronychia, anorexia, hypomagnesemia, hypokalemia, rash, acneiform dermatitis, pruritus, and dry skin. The most frequently reported serious adverse reactions are diarrhea and dehydration.

To see the full Vectibix Safety Information, visit www.vectibix.com.

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 one of the world's leading independent biotechnology companies, 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 the current expectations and beliefs of Amgen Inc. and its subsidiaries (Amgen, we or us) 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 Inc., including Amgen Inc.'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 Inc.'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 Jan. 15, 2015, 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 and our partners 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 (including products of our wholly-owned subsidiaries) 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 and our partners routinely obtain patents for our and their products and technology, the protection of our products offered by patents and patent applications may be challenged, invalidated or circumvented by our or our partners' competitors and there can be no guarantee of our or our partners' 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. Our efforts to integrate the operations of companies we have acquired may not be successful. Cost savings initiatives may result in us incurring impairment or other related charges on our assets. We may experience difficulties, delays or unexpected costs and not achieve anticipated benefits and savings from our recently announced restructuring plans. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or our ability to pay a dividend or repurchase common stock.

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, and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidates.

Avastin® is a registered trademark of Genentech, Inc.

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