# FDA Approves First-Line Use of Vectibix® (Panitumumab) Plus FOLFOX for Patients with Wild-Type KRAS Metastatic Colorectal Cancer

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**Vectibix is the First and Only Biologic to Offer Significant Survival Benefit as a First-Line Treatment with FOLFOX Chemotherapy for Patients with Wild-Type KRAS Metastatic Colorectal Cancer**
**Approval Reinforces Amgen Commitment to Personalized Medicine**

THOUSAND OAKS, Calif., May 23, 2014 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced that the U.S. Food and Drug Administration (FDA) has approved Vectibix® (panitumumab) for use in combination with FOLFOX, an oxaliplatin-based chemotherapy regimen, as first-line treatment in patients with wild-type *KRAS* (exon 2) metastatic colorectal cancer (mCRC). With this approval, Vectibix becomes the first and only biologic to offer a significant survival benefit as a first-line treatment with FOLFOX, one of the most commonly used chemotherapy regimens in the first-line setting for patients with wild-type *KRAS* mCRC. In addition, this approval converts the accelerated monotherapy approval to a full approval for Vectibix. FDA also approved the *therascreen*® *KRAS* RGQ PCR Kit developed by QIAGEN (*therascreen KRAS* test) as a companion diagnostic for Vectibix.

To view the multimedia assets associated with this release, please click: http://www.multivu.com/mnr/7061856-new-fda-indication-approved-for-amgen-s-vectibix

Today's announcement is the latest milestone in Amgen's pioneering cancer biomarker research, aimed at helping oncologists personalize cancer treatment to improve patient outcomes. Biomarkers are biological characteristics that demonstrate the likelihood of an individual's response or lack of response to a particular therapy and are a key element in personalized medicine that can help oncologists choose treatments for patients who are most likely to benefit.

"Because every patient with cancer is unique, we have made it our mission to focus on identifying treatment options for patients based on their cancer's genetic makeup," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "Approval of Vectibix in combination with FOLFOX for first-line treatment of patients with wild-type *KRAS* metastatic colorectal cancer is an example of the advancements that can be made through a greater understanding of distinct genetic markers associated with difficult-to-treat diseases."

The approval is based on results from Amgen's PRIME ('203) and ASPECCT ('763) trials. The PRIME Phase 3 study showed that patients with wild-type *KRAS* tumors in exon 2 achieved statistically significant improvement in progression-free survival (PFS) with Vectibix and FOLFOX versus FOLFOX alone (9.6 versus 8.0 months, $p$=0.02) and a significant 4.4 month improvement in overall survival (OS) versus FOLFOX alone (23.8 versus 19.4 months).

The Phase 3 ASPECCT study met its primary endpoint of non-inferiority for improving overall survival in patients taking Vectibix versus Erbitux® (cetuximab) as a single agent for the treatment of mCRC in patients with wild-type *KRAS* tumors who have not responded to chemotherapy.

"Vectibix is now the first approved biologic to show a significant survival benefit when combined with FOLFOX as a first-line treatment," said Lee S. Schwartzberg, M.D., medical director of The West Clinic, Memphis, Tenn. "Vectibix has shown a significant benefit to patients with wild-type *KRAS* metastatic colorectal cancer when used with FOLFOX, which gives us a valuable new treatment option as we help patients fight this devastating disease."

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.[3]

**About Vectibix® (panitumumab)**
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 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.

**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)].

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 (≥ 20%) in patients with wild-type KRAS mCRC receiving Vectibix (6 mg/kg every 2 weeks) and FOLFOX therapy (N = 322) in Study 3 were diarrhea, stomatitis, mucosal inflammation, asthenia, paronychia, anorexia, hypomagnesemia, hypokalemia, rash, acneiform dermatitis, pruritus, and dry skin. Serious adverse reactions (≥ 2% difference between treatment arms) in Vectibix-treated patients with wild-type KRAS mCRC were 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 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 the current expectations and beliefs of Amgen Inc. and its subsidiaries (Amgen 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 May 23, 2014 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 Amgen and its partners routinely obtain patents for 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.

The 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.

Erbitux® is a registered trademark of ImClone LLC.

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