Amgen Receives Positive CHMP Opinion For Use Of Vectibix® (panitumumab) As First-Line Treatment In Combination With FOLFIRI Chemotherapy For Advanced Colorectal Cancer

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THOUSAND OAKS, Calif., Feb. 27, 2015 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion to extend the marketing authorization for Vectibix® (panitumumab) to include combination with FOLFIRI (an irinotecan-based chemotherapy) as first-line treatment in adult patients with wild-type *RAS* metastatic colorectal cancer (mCRC). About half of the patients with mCRC have wild-type *RAS* tumors.[1]

"Adding Vectibix to chemotherapy as first-line treatment in patients with wild-type *RAS* metastatic colorectal cancer has been shown to result in better responses than chemotherapy alone," said Elliott M. Levy, M.D., senior vice president of Global Development at Amgen. "The CHMP recommendation is an important step toward increasing the treatment options for patients with this aggressive disease and helping improve outcomes in the European Union."

The new indication is based upon the 20060314 study, which evaluated Vectibix plus FOLFIRI in the first-line setting. Vectibix is already approved in the European Union (EU) for the treatment of adult patients with wild-type *RAS* mCRC[1]:

- 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.

The CHMP positive opinion will now be ratified by the European Commission who, should they affirm the CHMP opinion, will extend the centralized marketing authorization which is valid in the 28 countries that are members of the EU, as well as European Economic Area members, Iceland, Lichtenstein and Norway.

The safety profile of Vectibix was consistent with previously reported studies.

Colorectal cancer is the third most common cancer worldwide, with approximately 1.2 million cases expected to occur globally.[2,3] The highest estimated mortality rates associated with colorectal cancer occur in Central and Eastern Europe.[3]

About Vectibix® (panitumumab)

In the EU, Vectibix is currently indicated for the treatment of adult patients with wild-type *RAS* 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.

Important EU Product Safety Information

Dermatologic related reactions, a pharmacologic effect observed with epidermal growth factor receptor (EGFr) inhibitors, are experienced with nearly all patients (approximately 90 percent) treated with Vectibix. The majority of dermatological reactions are mild to moderate in nature. In clinical studies, subsequent to the development of severe dermatological reactions (including stomatitis), infectious complications including sepsis, in rare cases leading to death, and local abscesses requiring incisions and drainage were reported. Patients who have severe dermatologic reactions or who develop worsening reactions whilst receiving Vectibix should be monitored for the development of inflammatory or infectious sequelae, and appropriate treatment promptly initiated.

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 Study 3 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 (≥ 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 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 Feb. 27, 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. We may experience difficulties, delays or unexpected costs and not achieve anticipated benefits and savings from our recently announced restructuring plan. 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 relating to new indications for our products is preliminary and investigative and is not part of the labeling approved 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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[1] European Medicines Agency. Vectibix. http://www.ema.europa.eu/ema/index.jsp curl=pages/medicines/human/medicines/000741/human_med_001128.jsp&mid=WC0b01ac058001d124

[2] Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11. http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx. Accessed February 24, 2015.

[3] Jemal. Global Cancer Statistics. *CA Cancer J Clin*. 2011;61:69-90. Peeters M, Price TJ, Cervantes A, et al. Randomized Phase III Study of Panitumumab With Fluorouracil, Leucovorin, and Irinotecan (FOLFIRI) Compared with FOLFIRI Alone As Second-Line Treatment in Patients with Metastatic Colorectal Cancer. *J Clin Oncol.* 2010;28(31):4706-4713.

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