KRAS Gene Status May Impact Vectibix(TM) (Panitumumab) Efficacy and Patient Reported Outcomes in Advanced Colorectal Cancer Patients

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Data Presented at ASCO GI Further Validate KRAS as a Potential Patient Selection Biomarker for Vectibix Monotherapy

ABSTRACT NUMBER: 278

ORLANDO, Fla., Jan 24, 2008 (BUSINESS WIRE) -- Amgen (NASDAQ: AMGN) today announced the results of a biomarker analysis which indicated that in metastatic colorectal cancer (mCRC) patients who have failed all other chemotherapeutic regimens, the efficacy of Vectibix(TM) (panitumumab) monotherapy is confined to patients with non-mutated (wild-type) KRAS tumors. Specifically, in patients with non-mutated KRAS tumors, Vectibix significantly increased progression-free survival (PFS) and had an impact on quality of life (QoL) and disease-related symptoms, compared to best supportive care (BSC) alone. These data will be presented at an oral presentation on Saturday, January 26th at the 2008 American Society of Clinical Oncology Gastrointestinal Cancers Symposium (ASCO GI).

These data were generated from a biomarker analysis of a Phase 3, randomized, controlled clinical trial (the "408" study) that investigated the treatment effect of Vectibix monotherapy plus BSC versus BSC alone in patients with mCRC. The data showed the relative effect of Vectibix versus BSC was significantly greater in patients with non-mutated versus mutated KRAS (HR = 0.45 vs. HR = 0.99). Median PFS in patients without the mutation treated with Vectibix plus BSC was 12.3 weeks versus 7.3 weeks, respectively. When the analysis standardized the time to tumor assessment, the median PFS was 16 weeks versus 8 weeks, respectively (HR= 0.49 vs. 1.07). Some of these data were presented for the first time at the European Cancer Conference (ECCO) in September 2007.

"These data have substantially advanced our thinking about individualized treatment of colorectal cancers," said Roger M. Perlmutter, M.D., Ph.D., executive vice president of Research and Development at Amgen. "We are hopeful that the use of biomarkers like KRAS will enable improved treatment outcomes for colorectal cancer patients."

Additional endpoints of this analysis examined overall survival by KRAS status and treatment. When the treatment arms were combined (non-mutated vs. mutated) overall survival was longer in patients with non-mutated compared with mutated KRAS (HR = 0.67). No differences in overall survival were observed between Vectibix and BSC in either KRAS subgroup, potentially due to a high rate of crossover from BSC to Vectibix after progression, and similar efficacy of Vectibix in these patients.

In exploratory analyses, colorectal cancer symptoms and health-related quality of life (HRQoL) outcomes were compared between Vectibix and BSC treated patients using a validated instrument such as the Functional Assessment of Cancer Therapy-colorectal symptom index and HRQoL using the EQ-5D index, and the EORTC-QLQ-C30 Global Health Status. In patients with tumors carrying non-mutated KRAS genes, the analysis demonstrated that in Vectibix treated patients clinically meaningful inferior symptom control and QoL scores could be excluded compared to BSC, and that in fact, a clinically meaningful difference in favor of Vectibix was observed at most time points. In contrast, a clinically significant worsening of symptom control and QoL scores could not be excluded in patients with mutated KRAS tumors treated with Vectibix compared to BSC. The United States (U.S.) prescribing information states that the effectiveness of Vectibix as a single agent is based on progression-free survival; currently no data are available that demonstrate an improvement in disease-related symptoms or increased survival with Vectibix.

Over twenty years of study have shown that KRAS plays an important role in cell growth regulation and oncogenesis. Anti-epidermal growth factor receptor (EGFr) therapies work by blocking the activation of EGFr, thereby inhibiting downstream events that lead to cancer cell signaling. However, in patients with tumors harboring a mutated or activated KRAS, the KRAS protein is always turned "on" regardless of whether EGFr has been activated or therapeutically inhibited. Thus, in patients with mutated KRAS, signaling continues despite anti-EGFr therapy. Mutated KRAS is detected in approximately 40 percent of CRC tumors.

In the Vectibix-treated group, patients with non-mutated KRAS had on average double the number of Vectibix infusions as patients with mutated KRAS (10.0 vs. 4.9). Additionally, 20 percent of the KRAS evaluable patients had a treatment-related grade 3 adverse event (12 percent mutated vs. 25 percent non-mutated).

About the Analysis

Of the 463 randomized patients in the "408" trial, 427 had available KRAS data and 57 percent had tumors with normal, non-mutated KRAS. In the group of patients with non-mutated KRAS that received Vectibix, 17 percent responded to treatment and 34 percent reported stable disease. There were no responders in the group of patients treated with Vectibix that had mutated KRAS and stable disease was only reported in 12 percent of patients.

About Vectibix(TM)

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. In the U.S., Vectibix is not approved for use based on KRAS status. In December 2007, the European Medicines Agency (EMEA) granted a conditional marketing authorization for Vectibix as monotherapy for the treatment of patients with EGFr expressing mCRC with non-mutated (wild-type) KRAS genes after failure of standard chemotherapy regimens. Regulatory applications in the rest of the world are still pending.

KRAS and other biomarker analyses have and will continue to be integrated into the ongoing clinical program studying Vectibix in earlier lines of mCRC therapy in combination with chemotherapy, as well as in other tumor types. Emerging data from our ongoing Phase 3 trials examining Vectibix in combination with chemotherapy in the first- and second-line of mCRC (181 and 203) will be presented later at this meeting.

Important Product Safety Information

Dermatologic toxicities, related to Vectibix blockade of EGF binding and subsequent inhibition of EGF receptor-mediated signaling pathways, included but were not limited to dermatitis acneiform, pruritus, erythema, rash, skin exfoliation, paronychia, dry skin, and skin fissures. Dermatologic toxicities were reported in 89 percent of patients treated with Vectibix and were severe in 12 percent of patients. Severe dermatologic toxicities were complicated by infection, including sepsis, septic death, and abscesses requiring incisions and drainage. Vectibix may need to be withheld or discontinued for severe dermatologic toxicities.

Severe infusion reactions occurred with Vectibix in approximately 1 percent of patients. Severe infusion reactions were identified as anaphylactic reactions, bronchospasm, fever, chills, and hypotension. Although fatal infusion reactions have not been reported with Vectibix, they have occurred with other monoclonal antibody products. Severe infusion reactions require stopping the infusion and possibly permanently discontinuing Vectibix, depending on the severity and/or persistence of the reaction.

About Amgen

Amgen discovers, develops 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 and effective medicines from lab, to manufacturing plant, to patient. Amgen therapeutics have changed the practice of medicine, helping millions of people around the world in the fight against cancer, kidney disease, rheumatoid arthritis, and other serious illnesses. With a deep and broad pipeline of potential new medicines, Amgen remains committed to advancing science to dramatically improve people's lives. To learn more about our pioneering science and our vital medicines, visit www.amgen.com.

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 most recent 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. 25, 2007 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 products liability claims. 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 payors, 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 health care 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.

SOURCE: Amgen

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