KRAS Biomarker Analysis from Pivotal Vectibix(TM) Trial Published

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Manuscript Data Delineate Potential Role of KRAS Oncogene in Patient Selection for Vectibix Treatment

THOUSAND OAKS, Calif., Mar 04, 2008 (BUSINESS WIRE) -- Amgen (NASDAQ: AMGN) today announced that the results from a biomarker analysis of the pivotal "408" trial were published in the Journal of Clinical Oncology (JCO). The analysis showed that KRAS mutations could be used to identify patients who may not respond to treatment with Vectibix(TM) (panitumumab) monotherapy, the first fully human anti-epidermal growth factor receptor (EGFr) monoclonal antibody. These data were previously reported at the European Cancer Conference in 2007 and the Gastrointestinal Cancer Symposium in January 2008. The paper was made available early online on the JCO Web site and will be in the April 2008 print edition.

These findings are the first published results from a Phase 3 randomized, controlled clinical trial to affirm the link between non-mutated (wild-type) KRAS in tumors, and the efficacy of treatment with anti-EGFr in patients with metastatic colorectal cancer (mCRC). The analysis met primary and secondary endpoints by demonstrating that the effect of Vectibix on progression-free survival (PFS) was different in patients according to the mutational status of the KRAS gene in their tumors. The effect of Vectibix on PFS and response rate appeared to be confined exclusively to the patients whose tumors harbor normal, non-mutated KRAS.

"These results validate the importance of the KRAS oncogene in identifying appropriate patients for treatment with Vectibix monotherapy in the advanced colorectal cancer setting," said Roger M. Perlmutter, M.D., Ph.D., executive vice president of Research and Development at Amgen. "We have developed the first prospective clinical trials with KRAS in earlier lines of mCRC to enhance our understanding of this biomarker and its potential application. We also are continuing to investigate the role of other markers to further refine patient selection."

These analyses were derived from the pivotal "408" trial, which had shown that Vectibix monotherapy was significantly more effective than best supportive care in treating mCRC patients in the chemorefractory setting. Activating KRAS mutations were detected using real-time polymerase chain reaction (PCR) on DNA derived mostly from fixed, archived tumor sections.

About KRAS

Results from studies performed over the last twenty-five years indicate that KRAS plays an important role in cell growth regulation. In mCRC, the 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. Anti-EGFr therapies work by blocking the activation of EGFr, thereby inhibiting downstream events that lead to malignant signaling. However, it is hypothesized that in patients with tumors harboring a mutated KRAS gene, the KRAS protein is always turned "on," regardless of whether the EGFr has been activated or therapeutically inhibited.

About Vectibix

Vectibix was approved in the United States (U.S.) in September 2006 as a single agent 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 PFS. Currently no data are available that demonstrate an improvement in disease-related symptoms or increased survival with Vectibix. 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 KRAS genes after failure of standard chemotherapy regimens. Regulatory applications in the rest of the world are still pending.

There are currently ongoing Phase 3 trials examining Vectibix in combination with chemotherapy in the first- and second-line of mCRC. 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.

Important Product Safety Information - U.S.

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.

Important Product Safety Information - European Union

Dermatologic related reactions, a pharmacologic effect observed with 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.

About Amgen

Amgen discovers, develops, manufactures 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 March 4, 2008 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 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. 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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