Amgen Announces Overall Survival Results for Vectibix(R) in First-Line Metastatic Colorectal Cancer

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Phase 3 Results Reinforce Importance of KRAS Status

THOUSAND OAKS, Calif., Nov. 5 /PRNewswire-FirstCall/ -- Amgen (Nasdaq: AMGN) today announced that the Phase 3 PRIME "203" trial evaluating Vectibix (R) (panitumumab) administered in combination with FOLFOX (an oxaliplatin-based chemotherapy) as a first-line treatment of metastatic colorectal cancer (mCRC) failed to meet a secondary endpoint of overall survival. Earlier this year, it was announced that the trial met its primary endpoint by significantly prolonging progression-free survival (PFS) in the first-line treatment of patients with *KRAS* wild-type mCRC.

The prospective analysis of the 203 study showed that Vectibix, when added to a FOLFOX chemotherapy regimen in patients with *KRAS* wild-type mCRC, resulted in a median overall survival of 23.9 months compared to 19.7 months for patients treated with FOLFOX alone. The median overall survival difference of 4.2 months in the Vectibix arm did not reach statistical significance (HR=0.83, p=0.072).

"As we previously announced, the 203 study met its primary endpoint of progression-free survival in the first-line treatment of patients with *KRAS* wild-type metastatic colorectal cancer," said Roger M. Perlmutter, M.D., Ph.D., executive vice president of Research and Development at Amgen. "While not statistically significant, we are also encouraged by the positive trend of the data for overall survival for these patients treated with Vectibix."

Overall survival appeared to be reduced in patients with *KRAS* mutant tumors receiving Vectibix. Although not statistically significant, this result emphasizes the importance, as described in product labeling, of ensuring that patients receiving Vectibix( )do not bear tumors containing *KRAS* mutations.

Overall, the adverse event profile was as anticipated for an anti-EGFR antibody in combination with oxaliplatin-based chemotherapy, including known events such as rash, diarrhea and hypomagnesemia. Vectibix-related grade 3 infusion reactions were reported for two patients (less than 1 percent).

Originally designed to compare the treatment effect in the overall population, the study was amended to analyze outcomes with respect to the presence or absence of activating mutations in *KRAS* in the tumor itself. Tumor *KRAS* status was ascertained in more than 90 percent of the 1,183 patients enrolled in the trial.

Available results from the trial were presented earlier this year at the 2009 ECCO 15 - ESMO 34 European Multidisciplinary Congress in Berlin, Germany showing that Vectibix significantly improved median progression-free survival by 1.6 months (9.6 versus 8.0 months for patients treated with FOLFOX alone, in patients with *KRAS* wild-type mCRC (primary endpoint). Further, the addition of Vectibix to chemotherapy also improved response rate in the *KRAS* wild-type patient population as measured by blinded central review (55 percent versus 48 percent in the FOLFOX only arm).

The data for the 203 study has been submitted for consideration of presentation at the American Society of Clinical Oncology - The Gastrointestinal Cancers Symposium Meeting for 2010.

Study Design

Patients enrolled in the "203" or PRIME trial (Panitumumab Randomized trial in combination with chemotherapy for Metastatic colorectal cancer to determine Efficacy) were randomized to receive either 6.0 mg/kg of Vectibix and FOLFOX4 once every two weeks (Q2W) or FOLFOX4 alone Q2W. The primary endpoint of the study is progression-free survival by *KRAS* status and secondary endpoints include overall survival, objective response rate, time to progression, duration of response and safety.

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, 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 antibody therapies work by blocking the activation of EGFR, thereby inhibiting downstream events that lead to malignant signaling. However, it is hypothesized that in patients whose tumors harbor a mutated *KRAS* gene, the *KRAS* protein is always turned "on," regardless of whether the EGFR has been activated or therapeutically inhibited. *KRAS* mutations occur in approximately 40 - 50 percent of mCRC.

About Colorectal Cancer

Colorectal cancer is the fourth most common cancer in men and the third most common cancer in women worldwide. In 2007, approximately 1.2 million cases of colorectal cancer were expected to occur globally. With more than 630,000 deaths worldwide per year, it is the second leading cause of cancer-related death in the Western world. The highest incidence rates are found in Japan, North America, parts of Europe, New Zealand, and Australia, and rates are low in Africa and South-East Asia.( ) Rates are substantially higher in men than in women.

About Vectibix

Vectibix is the first fully human anti-EGFR antibody approved by the U.S. Food and Drug Administration (FDA) for the treatment of mCRC. Vectibix was approved in the United States 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.

The effectiveness of Vectibix as a single agent for the treatment of EGFR-expressing, metastatic colorectal carcinoma is based on progression-free survival. Currently no data are available that demonstrate an improvement in disease-related symptoms or increased survival with Vectibix. Vectibix has not shown a treatment benefit for patients whose tumors had *KRAS* mutations in codon 12 or 13.

In December 2007, the EMEA granted a conditional marketing authorization for Vectibix as monotherapy for the treatment of patients with EGFR-expressing mCRC with wild-type *KRAS* genes after failure of standard chemotherapy regimens. Vectibix has been launched in over 20

countries, Switzerland, Australia and Canada. Applications in the rest of the world are pending.

Important Product Safety Information

Dermatologic Toxicity: Dermatologic toxicities occurred in 89 percent of patients and were severe (NCI-CTC grade 3 and higher) in 12 percent of patients receiving Vectibix monotherapy. Withhold Vectibix for dermatologic toxicities that are grade 3 or higher or are considered intolerable. If toxicity does not improve to