Amgen Showcases New Data From Oncology Pipeline And Portfolio At ESMO 2019

September 17, 2019

New Data Show Clinical Responses in Colorectal and Appendiceal Cancer Patients Treated With AMG 510
Two Late-Breaking Abstracts With Data Highlighting IMLYGIC® (Talimogene Laherparepvec) for Neoadjuvant Melanoma and in Combination for Advanced Melanoma
Results From Studies Across Marketed Portfolio in Cancer Patients With Solid Tumors

THOUSAND OAKS, Calif., Sept. 17, 2019 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that new data from its oncology pipeline and marketed product portfolio will be presented at the European Society for Medical Oncology (ESMO) 2019 Congress in Barcelona, Spain, Sept. 27-Oct. 1, 2019.

Clinical data presentations will include a poster discussion on the ongoing Phase 1 trial of AMG 510, highlighting responses in *KRAS G12C*-mutant solid tumors, including patients with advanced non-small cell lung, colorectal and appendiceal cancers. AMG 510 is the first $KRAS^{G12C}$ inhibitor to reach the clinical stage in patients with locally advanced or metastatic *KRAS G12C*-mutated solid tumors.

Data showing the two-year results of a Phase 2 trial in patients with neoadjuvant melanoma being treated with IMLYGIC® (talimogene laherparepvec) plus surgery versus immediate surgery will be presented as a late-breaking abstract in an oral presentation. A second late-breaking abstract featuring IMLYGIC will be presented in a poster discussion session, highlighting three-year follow-up data of a Phase 2 trial with IMLYGIC in combination with YERVOY® (ipilimumab) for advanced melanoma.

"The data being presented at ESMO demonstrate how Amgen is advancing the next frontier of innovation in the treatment of cancers," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "In addition to the responses seen in non-small cell lung cancer patients with *KRAS G12C*-mutant tumors, we will report the first responses in advanced colorectal and appendiceal cancers at the upcoming congress."

A complete listing of abstracts can be found on the ESMO website. Notable abstracts of interest include:

Oncology Pipeline

- **Phase 1 Study of AMG 510, a Novel Molecule Targeting *KRAS G12C*-Mutant Solid Tumors**
  Abstract #446PD, Poster Discussion, Saturday, Sept. 28, session at 4:30 p.m. CEST, discussion at 4:52 p.m. CEST in Alicante Auditorium (Hall 3)

- **A Phase 1 Study of AMG 160, a Half-Life Extended Bispecific T-Cell Engager (HLE BiTE®) Immuno-Oncology Therapy Targeting PSMA, in Patients (pts) With Metastatic Castration-Resistant Prostate Cancer (mCRPC)**
  Abstract #895TiP, Poster Presentation, Monday, Sept. 30, at noon CEST in Poster Area (Hall 4), Fira Gran Via

IMLYGIC

- **Primary 2-Year Results of the Phase 2, Multicenter, Randomized, Open-Label Trial of Efficacy and Safety for Talimogene Laherparepvec (T-VEC) Neoadjuvant (neo) Treatment (tx) Plus Surgery vs. Immediate Surgery in Patients (pts) With Resectable Stage IIIB-IVM1a Melanoma**
  Abstract #LBA66, Oral Presentation, Saturday, Sept. 28, session and lecture at 8:30 a.m. CEST in Cordoba Auditorium (Hall 7)

- **Talimogene Laherparepvec (T-VEC) in Combination (combo) With Ipilimumab (ipi) Versus ipi Alone for Advanced Melanoma: 3-Year Landmark Analysis of a Randomized, Open-Label Phase 2 Trial**
  Abstract #LBA70, Poster Discussion, Saturday, Sept. 28, session and discussion at 2:45 p.m. CEST in Granada Auditorium (Hall 3)

- **Efficacy of Talimogene Laherparepvec (T-VEC) in Melanoma Patients (pts) With Locoregional Recurrence, Including In-transit Metastases (ITM): Subgroup Analysis of the Phase III OPTiM Study**
  Abstract #1342P, Poster Presentation, Monday, Sept. 30, at noon CEST in Poster Area (Hall 4), Fira Gran Via

XGEVA® (denosumab)

- **Use of Skeletal-Related Events Preventative Agents in Patients With Solid Tumors and Bone Metastases in Central Denmark**
  Abstract #1793P, Poster Presentation, Saturday, Sept. 28, at noon CEST in Poster Area (Hall 4), Fira Gran Via

- **Adherence to ESMO 2014 Guidelines on Bone-Targeting Agent Initiation for Breast and Prostate Cancer Patients: Real-World Insights From Practicing European Physicians**

Abstract #1792P, Poster Presentation, Saturday, Sept. 28, at noon CEST in Poster Area (Hall 4), Fira Gran Via

- **Patterns of Care for Patients With Metastatic Bone Disease in Solid Tumors – a Cross-Sectional Study (SAKK 95/16)**
  Abstract #1797P, Poster Presentation, Saturday, Sept. 28, at noon CEST in Poster Area (Hall 4), Fira Gran Via

- **Utilization Pattern of Bone Targeting Agents in Patients With Solid Tumor in Taiwan, Hong Kong and Korea**
  Abstract #379P, Poster Presentation, Sunday, Sept. 29, at noon CEST in Poster Area (Hall 4), Fira Gran Via

Vectibix® (panitumumab)

- **Sequential RAS Mutation Testing in cfDNA in RAS Wild Type (wt) Metastatic Colorectal Cancer (mCRC) Patients (p) Treated With Panitumumab (P) and Chemotherapy (CT) in First Line (1L) PERSEIDA Study**
  Abstract #531PD, Poster Discussion, Sunday, Sept. 29, session at 3 p.m. CEST, discussion at 3:25 p.m. CEST in Cordoba Atrium (Hall 7), Fira Gran Via

- **Early Tumour Shrinkage (ETS), Depth of Response (DpR) and Associated Survival Outcomes in Patients (pts) With RAS Wild Type (WT) Metastatic Colorectal Cancer (mCRC) Classified According to Köhne Prognostic Category: Retrospective Analysis of the Panitumumab (Pmab) PRIME Study**
  Abstract #572P, Poster Presentation, Sunday, Sept. 29, at noon CEST in Poster Area (Hall 4), Fira Gran Via

- **Middle East & North Africa Registry to Characterize RAS Mutation Status and Tumor Specifications in Recently Diagnosed Patients With Metastatic Colorectal Cancer (MORE-RAS Study)**
  Abstract #656P, Poster Presentation, Sunday, Sept. 29, at noon CEST in Poster Area (Hall 4), Fira Gran Via

- **Quality of Life During 1st-Line FOLFOXIRI+/- Panitumumab in RAS Wild-type Metastatic Colorectal Cancer: Results From the Randomized VOLFI Trial (AIO KRK-0109)**
  Abstract #580P, Poster Presentation, Sunday, Sept. 29, at noon CEST in Poster Area (Hall 4), Fira Gran Via

- **Final Results of a Phase II Study of Induction Chemotherapy (CT) With Paclitaxel (PTX) and Panitumumab (P) Followed by Radiotherapy (RT) and P in Patients (pts) With Locally Advanced Head and Neck Cancer (LAHNC) No Candidates to Platinum: Study PANTERA**
  Abstract #1128P, Poster Presentation, Monday, Sept. 30, at noon CEST in Poster Area (Hall 4), Fira Gran Via

About *KRAS*

The subject of more than three decades of research, the *RAS* gene family are the most frequently mutated oncogenes in human cancers.[1,2] Within this family, *KRAS* is the most prevalent variant and is particularly common in solid tumors.[2] A specific mutation known as *KRAS G12C* accounts for approximately 13% of non-small cell lung cancers, three to five percent of colorectal cancers and one to two percent of numerous other solid tumors.[3] Approximately 30,000 patients are diagnosed each year in the United States (U.S.) with *KRAS G12C*-driven cancers.[4] $KRAS^{G12C}$ has been considered "undruggable" due to a lack of traditional small molecule binding pockets on the protein. Amgen is exploring the potential of $KRAS^{G12C}$ inhibition across a broad variety of tumor types.

About BiTE® Technology

Bispecific T cell engager (BiTE®) technology is a targeted immuno-oncology platform that is designed to engage patients' own T cells to any tumor-specific antigen, activating the cytotoxic potential of T cells to eliminate detectable cancer. The BiTE immuno-oncology platform has the potential to treat different tumor types through tumor-specific antigens. The BiTE platform leads to off-the-shelf solutions, which have the potential to make innovative T cell treatment available to all providers when their patients need it. Amgen is advancing more than a dozen BiTE molecules across a broad range of hematologic malignancies and solid tumors, further investigating BiTE technology with the goal of enhancing patient experience and therapeutic potential.

About IMLYGIC® (talimogene laherparepvec)

IMLYGIC is a genetically modified herpes simplex type 1 virus that is injected directly into tumors. IMLYGIC replicates inside tumor cells and produces GM-CSF, an immunostimulatory protein. IMLYGIC then causes the cell to rupture and die in a process called lysis. The rupture of the cancer cells causes the release of tumor-derived antigens, which together with virally derived GM-CSF may help to promote an anti-tumor immune response. However, the exact mechanism of action is unknown.

IMLYGIC is the first oncolytic viral therapy approved by the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) based on therapeutic benefit demonstrated in a pivotal study. IMLYGIC is a genetically modified oncolytic viral therapy indicated for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery. IMLYGIC has not been shown to improve overall survival (OS) or have an effect on visceral metastases.

INDICATION & LIMITATIONS OF USE

IMLYGIC® (talimogene laherparepvec) is a genetically modified oncolytic viral therapy indicated for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery.

Limitations of use: IMLYGIC® has not been shown to improve overall survival or have an effect on visceral metastases.

IMPORTANT SAFETY INFORMATION

Contraindications

- Do not administer IMLYGIC® to immunocompromised patients, including those with a history of primary or acquired immunodeficient states, leukemia, lymphoma, AIDS or other clinical manifestations of infection with human immunodeficiency viruses, and those on immunosuppressive therapy, due to the risk of life-threatening disseminated herpetic infection.
- Do not administer IMLYGIC® to pregnant patients.

Warnings and Precautions

- Accidental exposure to IMLYGIC® may lead to transmission of IMLYGIC® and herpetic infection, including during preparation and administration. Health care providers, close contacts, pregnant women, and newborns should avoid direct contact with injected lesions, dressings, or body fluids of treated patients. The affected area in exposed individuals should be cleaned thoroughly with soap and water and/or a disinfectant.
- Caregivers should wear protective gloves when assisting patients in applying or changing occlusive dressings and observe safety precautions for disposal of used dressings, gloves, and cleaning materials. Exposed individuals should clean the affected area thoroughly with soap and water and/or a disinfectant.
- To prevent possible inadvertent transfer of IMLYGIC® to other areas of the body, patients should be advised to avoid touching or scratching injection sites or occlusive dressings.
- Herpetic infections: Herpetic infections (including cold sores and herpetic keratitis) have been reported in IMLYGIC®-treated patients. Disseminated herpetic infection may also occur in immunocompromised patients. Patients who develop suspicious herpes-like lesions should follow standard hygienic practices to prevent viral transmission.
- Patients or close contacts with suspected signs or symptoms of a herpetic infection should contact their health care provider to evaluate the lesions. Suspected herpetic lesions should be reported to Amgen at 1-855-IMLYGIC (1-855-465-9442). Patients or close contacts have the option of follow-up testing for further characterization of the infection.
- IMLYGIC® is sensitive to acyclovir. Acyclovir or other antiviral agents may interfere with the effectiveness of IMLYGIC®. Consider the risks and benefits of IMLYGIC® treatment before administering antiviral agents to manage herpetic infection.
- Injection Site Complications: Necrosis or ulceration of tumor tissue may occur during IMLYGIC® treatment. Cellulitis and systemic bacterial infection have been reported in clinical studies. Careful wound care and infection precautions are recommended, particularly if tissue necrosis results in open wounds.
- Impaired healing at the injection site has been reported. IMLYGIC® may increase the risk of impaired healing in patients with underlying risk factors (eg, previous radiation at the injection site or lesions in poorly vascularized areas). If there is persistent infection or delayed healing of the injection site, consider the risks and benefits of continuing treatment.
- Immune-Mediated events including glomerulonephritis, vasculitis, pneumonitis, worsening psoriasis, and vitiligo have been reported in patients treated with IMLYGIC®. Consider the risks and benefits of IMLYGIC® before initiating treatment in patients who have underlying autoimmune disease or before continuing treatment in patients who develop immune-mediated events.
- Plasmacytoma at the Injection Site: Plasmacytoma in proximity to the injection site has been reported in a patient with smoldering multiple myeloma after IMLYGIC® administration in a clinical study. Consider the risks and benefits of IMLYGIC® in patients with multiple myeloma or in whom plasmacytoma develops during treatment.
- Obstructive Airway Disorder: Obstructive airway disorder has been reported following IMLYGIC® treatment. Use caution when injecting lesions close to major airways.

Adverse Reactions

- The most commonly reported adverse drug reactions (≥ 25%) in IMLYGIC®-treated patients were fatigue, chills, pyrexia, nausea, influenza-like illness, and injection site pain. Pyrexia, chills, and influenza-like illness can occur at any time during IMLYGIC® treatment, but were more frequent during the first 3 months of treatment.
- The most common Grade 3 or higher adverse reaction was cellulitis.

Please see www.Imlygic.com for full Prescribing Information, including Medication Guide.

About XGEVA® (denosumab)
XGEVA targets the RANKL pathway to prevent the formation, function and survival of osteoclasts, which break down bone. XGEVA is indicated for the prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors. XGEVA is also indicated for treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity and for the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.

INDICATIONS

XGEVA® is indicated for the prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors. XGEVA® is indicated for treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity. XGEVA® is indicated for the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.

IMPORTANT SAFETY INFORMATION

Important Safety Information

Hypocalcemia

Pre-existing hypocalcemia must be corrected prior to initiating therapy with XGEVA®. XGEVA® can cause severe symptomatic hypocalcemia, and fatal cases have been reported. Monitor calcium levels, especially in the first weeks of initiating therapy, and administer calcium, magnesium, and vitamin D as necessary. Monitor levels more frequently when XGEVA® is administered with other drugs that can also lower calcium levels. Advise patients to contact a healthcare professional for symptoms of hypocalcemia.

An increased risk of hypocalcemia has been observed in clinical trials of patients with increasing renal dysfunction, most commonly with severe dysfunction (creatinine clearance less than 30 mL/minute and/or on dialysis), and with inadequate/no calcium supplementation. Monitor calcium levels and calcium and vitamin D intake.

Hypersensitivity

XGEVA® is contraindicated in patients with known clinically significant hypersensitivity to XGEVA®, including anaphylaxis that has been reported with use of XGEVA®. Reactions may include hypotension, dyspnea, upper airway edema, lip swelling, rash, pruritus, and urticaria. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue XGEVA® therapy permanently.

Drug Products with Same Active Ingredient

Patients receiving XGEVA® should not take Prolia® (denosumab).

Osteonecrosis of the Jaw

Osteonecrosis of the jaw (ONJ) has been reported in patients receiving XGEVA®, manifesting as jaw pain, osteomyelitis, osteitis, bone erosion, tooth or periodontal infection, toothache, gingival ulceration, or gingival erosion. Persistent pain or slow healing of the mouth or jaw after dental surgery may also be manifestations of ONJ. In clinical trials in patients with cancer, the incidence of ONJ was higher with longer duration of exposure.

Patients with a history of tooth extraction, poor oral hygiene, or use of a dental appliance are at a greater risk to develop ONJ. Other risk factors for the development of ONJ include immunosuppressive therapy, treatment with angiogenesis inhibitors, systemic corticosteroids, diabetes, and gingival infections.

Perform an oral examination and appropriate preventive dentistry prior to the initiation of XGEVA® and periodically during XGEVA® therapy. Advise patients regarding oral hygiene practices. Avoid invasive dental procedures during treatment with XGEVA®. Consider temporarily interrupting XGEVA® therapy if an invasive dental procedure must be performed.

Patients who are suspected of having or who develop ONJ while on XGEVA® should receive care by a dentist or an oral surgeon. In these patients, extensive dental surgery to treat ONJ may exacerbate the condition.

Atypical Subtrochanteric and Diaphyseal Femoral Fracture

Atypical femoral fracture has been reported with XGEVA®. These fractures can occur anywhere in the femoral shaft from just below the lesser trochanter to above the supracondylar flare and are transverse or short oblique in orientation without evidence of comminution.

Atypical femoral fractures most commonly occur with minimal or no trauma to the affected area. They may be bilateral and many patients report prodromal pain in the affected area, usually presenting as dull, aching thigh pain, weeks to months before a complete fracture occurs. A number of reports note that patients were also receiving treatment with glucocorticoids (e.g. prednisone) at the time of fracture. During XGEVA® treatment, patients should be advised to report new or unusual thigh, hip, or groin pain. Any patient who presents with thigh or groin pain should be suspected of having an atypical fracture and should be evaluated to rule out an incomplete femur fracture. Patients presenting with an atypical femur fracture should also be assessed for symptoms and signs of fracture in the contralateral limb. Interruption of XGEVA® therapy should be considered, pending a risk/benefit assessment, on an individual basis.

Hypercalcemia Following Treatment Discontinuation in Patients with Giant Cell Tumor of Bone (GCTB) and in Patients with Growing Skeletons

Clinically significant hypercalcemia requiring hospitalization and complicated by acute renal injury has been reported in XGEVA®-treated patients with GCTB and in patients with growing skeletons within one year of treatment discontinuation. Monitor patients for signs and symptoms of hypercalcemia after treatment discontinuation and treat appropriately.

Multiple Vertebral Fractures (MVF) Following Treatment Discontinuation

Multiple vertebral fractures (MVF) have been reported following discontinuation of treatment with denosumab. Patients at higher risk for MVF include those with risk factors for or a history of osteoporosis or prior fractures. When XGEVA® treatment is discontinued, evaluate the individual patient's risk for vertebral fractures.

Embryo-Fetal Toxicity

XGEVA® can cause fetal harm when administered to a pregnant woman. Based on findings in animals, XGEVA® is expected to result in adverse reproductive effects.

Advise females of reproductive potential to use effective contraception during therapy, and for at least 5 months after the last dose of XGEVA®. Apprise the patient of the potential hazard to a fetus if XGEVA® is used during pregnancy or if the patient becomes pregnant while patients are

exposed to XGEVA®.

Adverse Reactions

The most common adverse reactions in patients receiving XGEVA® with bone metastasis from solid tumors were fatigue/asthenia, hypophosphatemia, and nausea. The most common serious adverse reaction was dyspnea. The most common adverse reactions resulting in discontinuation were osteonecrosis and hypocalcemia.

For multiple myeloma patients receiving XGEVA®, the most common adverse reactions were diarrhea, nausea, anemia, back pain, thrombocytopenia, peripheral edema, hypocalcemia, upper respiratory tract infection, rash, and headache. The most common serious adverse reaction was pneumonia. The most common adverse reaction resulting in discontinuation of XGEVA® was osteonecrosis of the jaw.

The most common adverse reactions in patients receiving XGEVA® for giant cell tumor of bone were arthralgia, headache, nausea, back pain, fatigue, and pain in extremity. The most common serious adverse reactions were osteonecrosis of the jaw and osteomyelitis.

The most common adverse reactions resulting in discontinuation of XGEVA® were osteonecrosis of the jaw and tooth abscess or tooth infection.

The most common adverse reactions in patients receiving XGEVA® for hypercalcemia of malignancy were nausea, dyspnea, decreased appetite, headache, peripheral edema, vomiting, anemia, constipation, and diarrhea.

Please visit www.xgeva.com for Full U.S. Prescribing Information.

About Vectibix® (panitumumab)

Vectibix is the first fully human monoclonal anti-EGFR antibody approved by the 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.

In June 2017, the FDA approved a refined indication for Vectibix for use in in patients with wild-type *RAS* (defined as wild-type in both *KRAS* and *NRAS* as determined by an FDA-approved test for this use*)* mCRC.

INDICATION AND LIMITATION OF USE

Vectibix® is indicated for the treatment of patients with wild-type *RAS* (defined as wild-type in both *KRAS* and *NRAS* as determined by an FDA-approved test for this use) metastatic colorectal cancer (mCRC): as first-line therapy in combination with FOLFOX, and as monotherapy following disease progression after prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy.

Limitation of Use: Vectibix® is not indicated for the treatment of patients with *RAS*-mutant mCRC or for whom *RAS* mutation status is unknown.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: DERMATOLOGIC TOXICITY

Dermatologic Toxicity: Dermatologic toxicities occurred in 90% of patients and were severe (NCI-CTC grade 3 and higher) in 15% of patients receiving Vectibix monotherapy *[see Dosage and Administration (2.3), Warnings and Precautions (5.1), and Adverse Reactions (6.1)].*

- In Study 20020408, dermatologic toxicities occurred in 90% of patients and were severe (NCI-CTC grade 3 and higher) in 15% of patients with mCRC receiving Vectibix®. The clinical manifestations included, but were not limited to, acneiform dermatitis, pruritus, erythema, rash, skin exfoliation, paronychia, dry skin, and skin fissures.

- Monitor patients who develop dermatologic or soft tissue toxicities while receiving Vectibix® for the development of inflammatory or infectious sequelae. Life-threatening and fatal infectious complications including necrotizing fasciitis, abscesses, and sepsis have been observed in patients treated with Vectibix®. Life-threatening and fatal bullous mucocutaneous disease with blisters, erosions, and skin sloughing has also been observed in patients treated with Vectibix®. It could not be determined whether these mucocutaneous adverse reactions were directly related to EGFR inhibition or to idiosyncratic immune- related effects (eg, Stevens Johnson syndrome or toxic epidermal necrolysis). Withhold or discontinue Vectibix® for dermatologic or soft tissue toxicity associated with severe or life-threatening inflammatory or infectious complications. Dose modifications for Vectibix® concerning dermatologic toxicity are provided in the product labeling.

- Vectibix® is not indicated for the treatment of patients with colorectal cancer that harbor somatic *RAS* mutations in 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 hereafter is referred to as "*RAS.*"

- Retrospective subset analyses across several randomized clinical trials were conducted to investigate the role of *RAS* mutations on the clinical effects of anti-EGFR-directed monoclonal antibodies (panitumumab or cetuximab). Anti-EGFR antibodies in patients with tumors containing *RAS* mutations resulted in exposing those patients to anti-EGFR related adverse reactions without clinical benefit from these agents. Additionally, in Study 20050203, 272 patients with *RAS*-mutant

mCRC tumors received Vectibix® in combination with FOLFOX and 276 patients received FOLFOX alone. In an exploratory subgroup analysis, OS was shorter (HR = 1.21, 95% CI: 1.01-1.45) in patients with *RAS*-mutant mCRC who received Vectibix® and FOLFOX versus FOLFOX alone.

- Progressively decreasing serum magnesium levels leading to severe (grade 3-4) hypomagnesemia occurred in up to 7% (in Study 20080763) 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. Other electrolyte disturbances, including hypokalemia, have also been observed. Replete magnesium and other electrolytes as appropriate.
- In Study 20020408, 4% of patients experienced infusion reactions and 1% of patients experienced severe infusion reactions (NCI-CTC grade 3-4). Infusion reactions, manifesting as fever, chills, dyspnea, bronchospasm, and hypotension, can occur following Vectibix® administration. Fatal infusion reactions occurred in postmarketing experience. Terminate the infusion for severe infusion reactions.
- 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 nonfatal 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.
- In patients with a history of interstitial pneumonitis or pulmonary fibrosis, or evidence of interstitial pneumonitis or pulmonary fibrosis, the benefits of therapy with Vectibix® versus the risk of pulmonary complications must be carefully considered.
- Exposure to sunlight can exacerbate dermatologic toxicity. Advise patients to wear sunscreen and hats and limit sun exposure while receiving Vectibix®.
- Keratitis and ulcerative keratitis, known risk factors for corneal perforation, have been reported with Vectibix® use. Monitor for evidence of keratitis or ulcerative keratitis. Interrupt or discontinue Vectibix® for acute or worsening keratitis.
- In an interim analysis of an open-label, multicenter, randomized clinical trial in the first-line setting in patients with mCRC, the addition of Vectibix® to the combination of bevacizumab and chemotherapy resulted in decreased OS and increased incidence of NCI-CTC grade 3-5 (87% vs 72%) adverse reactions. NCI-CTC grade 3-4 adverse reactions occurring at a higher rate in Vectibix®-treated patients included rash/acneiform dermatitis (26% vs 1%), diarrhea (23% vs 12%), dehydration (16% vs 5%), primarily occurring in patients with diarrhea, hypokalemia (10% vs 4%), stomatitis/mucositis (4% vs < 1%), and hypomagnesemia (4% vs 0).
- NCI-CTC grade 3-5 pulmonary embolism occurred at a higher rate in Vectibix®-treated patients (7% vs 3%) and included fatal events in three (< 1%) Vectibix®-treated patients. As a result of the toxicities experienced, patients randomized to Vectibix®, bevacizumab, and chemotherapy received a lower mean relative dose intensity of each chemotherapeutic agent (oxaliplatin, irinotecan, bolus 5-FU, and/or infusional 5-FU) over the first 24 weeks on study compared with those randomized to bevacizumab and chemotherapy.
- Vectibix® can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment, and for at least 2 months after the last dose of Vectibix®.
- In monotherapy, the most commonly reported adverse reactions (≥ 20%) in patients with Vectibix® were skin rash with variable presentations, paronychia, fatigue, nausea, and diarrhea.
- The most commonly reported adverse reactions (≥ 20%) with Vectibix® + FOLFOX were diarrhea, stomatitis, mucosal inflammation, asthenia, paronychia, anorexia, hypomagnesemia, hypokalemia, rash, acneiform dermatitis, pruritus, and dry skin. The most common serious adverse reactions (≥ 2% difference between treatment arms) were diarrhea and dehydration.

To see the Vectibix® Prescribing Information, including Boxed Warning visit www.vectibix.com.

About Amgen Oncology
Amgen Oncology is searching for and finding answers to incredibly complex questions that will advance care and improve lives for cancer patients and

their families. Our research drives us to understand the disease in the context of the patient's life – not just their cancer journey – so they can take control of their lives.

For the last four decades, we have been dedicated to discovering the firsts that matter in oncology and to finding ways to reduce the burden of cancer. Building on our heritage, Amgen continues to advance the largest pipeline in the Company's history, moving with great speed to advance those innovations for the patients who need them.

At Amgen, we are driven by our commitment to transform the lives of cancer patients and keep them at the center of everything we do.

For more information, follow us on www.twitter.com/amgenoncology.

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 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. 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 reports filed by Amgen, including our most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and current reports on Form 8-K. Unless otherwise noted, Amgen is providing this information as of the date of this news release and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

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. Even when clinical trials are successful, regulatory authorities may question the sufficiency for approval of the trial endpoints we have selected. 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, including our devices, after they are on the market.

Our results may be affected by our ability to successfully market both new and existing products domestically and internationally, clinical and regulatory developments involving current and future products, sales growth of recently launched products, competition from other products including biosimilars, difficulties or delays in manufacturing our products and global economic conditions. In addition, sales of our products are affected by pricing pressure, political and public scrutiny and 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. Furthermore, our research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. Our business may be impacted by government investigations, litigation and product liability claims. In addition, our business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. 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. Further, 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, or we may fail to prevail in present and future intellectual property litigation. We perform a substantial amount of our commercial manufacturing activities at a few key facilities, including in Puerto Rico, and also depend on third parties for a portion of our manufacturing activities, and limits on supply may constrain sales of certain of our current products and product candidate development. We rely on collaborations with third parties for the development of some of our product candidates and for the commercialization and sales of some of our commercial products. In addition, we compete with other companies with respect to many of our marketed products as well as for the discovery and development of new products. Further, some raw materials, medical devices and component parts for our products are supplied by sole third-party suppliers. Certain of our distributors, customers and payers have substantial purchasing leverage in their dealings with us. 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 acquire other companies or products and to integrate the operations of companies we have acquired may not be successful. A breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of our systems and our data. Our stock price is volatile and may be affected by a number of events. 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 our common stock. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all.

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 & Drug Administration or the European Medicines Agency 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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