Amgen Data To Be Presented At ASCO 2016 Demonstrates More Insights Into Treatment Options For Patients

May 18, 2016

New Analysis From Phase 3 Trial of Kyprolis® (Carfilzomib) Combination Treatment in Relapsed Multiple Myeloma Patients With Early Disease Progression

Phase 1/3 MASTERKEY-265 Study Abstracts Present Data on IMLYGIC® (Talimogene Laherparepvec) in Combination With Pembrolizumab in Patients With Unresected Stage IIIB-IV Melanoma

THOUSAND OAKS, Calif., May 18, 2016 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that new clinical data from across the oncology portfolio, including Kyprolis® (carfilzomib), IMLYGIC® (talimogene laherparepvec), Vectibix® (panitumumab) and Neulasta® (pegfilgrastim) will be presented at the 52nd Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago, June 3-7, 2016.

"As a leader in patient-focused oncology research, Amgen is committed to translating innovative science into treatments that make a difference in the lives of people suffering from cancer," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "The breadth and depth of data we're presenting at ASCO demonstrates our commitment to finding solutions to some of the toughest cancers. We are thankful for our research partners who help us achieve this mission, and we look forward to sharing these results at ASCO."

Amongst the Kyprolis abstracts to be presented at the meeting will be a new subgroup analysis from the Phase 3 ASPIRE trial which compared Kyprolis in combination with lenalidomide and dexamethasone versus lenalidomide and dexamethasone alone in relapsed multiple myeloma patients who had early disease progression following prior therapy (including transplant).

Presentations highlighting Kyprolis data include:

- **Carfilzomib, Lenalidomide, and Dexamethasone (KRd) vs. Lenalidomide and Dexamethasone (Rd) in Patients with Relapsed Multiple Myeloma (RMM) and Early Progression During Prior Therapy: Secondary Analysis From the Phase 3 Study ASPIRE (NCT01080391)**
  Abstract #8045, Poster, Monday, June 6 at 8 a.m. CDT in McCormick Place, Hall A
- **Risk of Hypertension (HTN) and Malignant Hypertension (mHTN) in Patients Treated for Multiple Myeloma (MM)**
  Abstract #8049, Poster, Monday, June 6 at 8 a.m. CDT in McCormick Place, Hall A
- **Transitions Across Different Lines of Therapy in the Medicare-Enrolled Patient Population with Multiple Myeloma**
  Abstract #8043, Poster, Monday, June 6 at 8 a.m. CDT in McCormick Place, Hall A
- **Treatment Regimens and Duration of Lines of Therapy in Medicare-Enrolled Patients with Multiple Myeloma**
  Abstract #8046, Poster, Monday, June 6 at 8 a.m. CDT in McCormick Place, Hall A
- **Costs Associated With Treatment Induced Peripheral Neuropathy in Patients with Multiple Myeloma (MM)**
  Abstract #8048, Poster, Monday, June 6 at 8 a.m. CDT in McCormick Place, Hall A
- **Healthcare Costs Among Multiple Myeloma (MM) Patients (Pts) without Stem Cell Transplant (SCT)**
  Abstract #8059, Poster, Monday, June 6 at 8 a.m. CDT in McCormick Place, Hall A
- **Retrospective Study of Frequency and Cost of Multiple Myeloma (MM) Complications and Treatment (Tx) Related Adverse Events (AEs)**
  Abstract #8060, Poster, Monday, June 6 at 8 a.m. CDT in McCormick Place, Hall A
- **Economic Evaluation of Carfilzomib + Lenalidomide + Dexamethasone (KRd) vs. Lenalidomide + Dexamethasone (Rd) in Relapsed or Refractory Multiple Myeloma (R/RMM)**
  Abstract #8021, Poster Discussion, Monday, June 6 at 3 p.m. CDT in McCormick Place, E354b

Two abstracts on the MASTERKEY-265 trial of IMLYGIC in combination with pembrolizumab in patients with unresectable Stage IIIB-IV melanoma will be presented:

- **Efficacy Analysis of MASTERKEY-265 Phase 1b Study of Talimogene Laherparepvec (T-VEC) and Pembrolizumab (Pembro) for Unresectable Stage IIIB-IV Melanoma**
  Abstract #9568, Poster Presentation, Saturday, June 4 from 1-4:30 p.m. CDT in McCormick Place, Hall A
- **A Phase 1/3, Multicenter Trial of Talimogene Laherparepvec in Combination with Pembrolizumab for Unresected, Stage IIIB-IV Melanoma (MASTERKEY-265)**
  Abstract #TPS9598, Poster Presentation, Saturday, June 4 from 1-4:30 p.m. CDT in McCormick Place, Hall A

Key data from two abstracts and one publication will be presented on Vectibix, including the final results from a Phase 3 trial of Vectibix and best supportive care (BSC) versus BSC in chemorefractory wild-type *KRAS* exon 2 and wild-type *RAS* metastatic colorectal cancer *(*mCRC):

- **Association of ECOG Performance Status with Efficacy in Patients Receiving Panitumumab with Best Supportive Care (BSC) vs. BSC Alone for Chemorefractory Metastatic Colorectal Cancer**
  Publication only

- **Final Results from a Phase 3 Trial Evaluating Panitumumab (pmab) + Best Supportive Care (BSC) vs. BSC in Chemorefractory Wild-type (WT) *KRAS* Exon 2 and WT *RAS* Metastatic Colorectal Cancer (mCRC)**
  Abstract #3536, Poster, Saturday, June 4 at 8 a.m. CDT in McCormick Place, Hall A
- **Efficacy of Panitumumab vs. Cetuximab in Patients with Wild-type *KRAS* Exon 2 Metastatic Colorectal Cancer Treated with Prior Bevacizumab: Results from ASPECCT**
  Abstract #3538, Poster, Saturday, June 4 at 8 a.m. CDT in McCormick Place, Hall A

Three abstracts will be presented on Neulasta and NEUPOGEN® (filgrastim), providing new insights into their role in supportive care, including:

- **NOLAN: A Randomized, Phase 2 Study to Estimate the Effect of Prophylactic Naproxen (N) or Loratadine (L) vs. No Intervention on Bone Pain in 600 Patients (pts) with Early-Stage Breast Cancer Receiving Chemotherapy (chemo) and Pegfilgrastim (PEG)**
  Abstract #10021, Poster Discussion, Monday, June 6 at 4:45 p.m. CDT in McCormick Place, S102
- **Burden of Febrile Neutropenia Hospitalizations (FNH) in U.S. Clinical Practice, by Use and Patterns of Colony-Stimulating Factor Prophylaxis (CP)**
  Abstract #6568, Poster, Saturday, June 4 at 1 p.m. CDT in McCormick Place, Hall A
- **Risk Factors for Febrile Neutropenia in Cancer Patients Treated With Chemotherapy**
  Abstract #6559, Poster, Saturday, June 4 at 1 p.m. CDT in McCormick Place, Hall A

One abstract will be presented on investigational agent ABP 215, which is being developed as a biosimilar to bevacizumab:

- **Randomized, Double-Blind, Phase 3 Study Evaluating Efficacy and Safety of ABP 215 Compared with Bevacizumab in Patients with Non-Squamous NSCLC**
  Abstract #9095, Poster Presentation, Saturday, June 4, at 8 a.m. CDT in McCormick Place, Hall A

Abstracts are currently available on the ASCO website.

About Kyprolis® (carfilzomib)

Proteasomes play an important role in cell function and growth by breaking down proteins that are damaged or no longer needed.[1] Kyprolis has been shown to block proteasomes, leading to an excessive build-up of proteins within cells.[2] In some cells, Kyprolis can cause cell death, especially in myeloma cells because they are more likely to contain a higher amount of abnormal proteins.[2] The irreversibility of Kyprolis' binding has also been shown to offer a more sustained inhibition of the targeted enzymes.[3]

Kyprolis is approved in the U.S. for the following:

- In combination with dexamethasone or with lenalidomide plus dexamethasone for the treatment of patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy.
- As a single agent for the treatment of patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy.

Kyprolis is also approved in Argentina, Israel, Kuwait, Mexico, Thailand, Colombia, Korea, Canada and the European Union. Additional regulatory applications for Kyprolis are underway and have been submitted to health authorities worldwide.

Kyprolis is a product of Onyx Pharmaceuticals, Inc. Onyx Pharmaceuticals is a subsidiary of Amgen and holds development and commercialization rights to Kyprolis globally, excluding Japan.

For more information, please visit www.kyprolis.com.

Important Safety Information Regarding Kyprolis® (carfilzomib) for Injection

INDICATION(S)

- KYPROLIS® (carfilzomib) is indicated in combination with dexamethasone or with lenalidomide plus dexamethasone for the treatment of patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy.
- KYPROLIS® (carfilzomib) is indicated as a single agent for the treatment of patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy.

IMPORTANT SAFETY INFORMATION

Cardiac Toxicities

- New onset or worsening of pre-existing cardiac failure (e.g., congestive heart failure, pulmonary edema, decreased ejection fraction), restrictive cardiomyopathy, myocardial ischemia, and myocardial infarction including fatalities have occurred following administration of KYPROLIS. Some events occurred in patients with normal baseline ventricular function. Death due to cardiac arrest has occurred within one day of KYPROLIS administration.
- Monitor patients for clinical signs or symptoms of cardiac failure or cardiac ischemia. Evaluate promptly if cardiac toxicity is

suspected. Withhold KYPROLIS for Grade 3 or 4 cardiac adverse events until recovery, and consider whether to restart KYPROLIS at 1 dose level reduction based on a benefit/risk assessment.
- While adequate hydration is required prior to each dose in Cycle 1, monitor all patients for evidence of volume overload, especially patients at risk for cardiac failure. Adjust total fluid intake as clinically appropriate in patients with baseline cardiac failure or who are at risk for cardiac failure.
- In Patients ≥ 75 years, the risk of cardiac failure is increased. Patients with New York Heart Association Class III and IV heart failure, recent myocardial infarction, conduction abnormalities, angina, or arrhythmias may be at greater risk for cardiac complications and should have a comprehensive medical assessment (including blood pressure and fluid management) prior to starting treatment with KYPROLIS and remain under close follow-up.

Acute Renal Failure

- Cases of acute renal failure and renal insufficiency adverse events (including renal failure) have occurred in patients receiving KYPROLIS. Acute renal failure was reported more frequently in patients with advanced relapsed and refractory multiple myeloma who received KYPROLIS monotherapy. Monitor renal function with regular measurement of the serum creatinine and/or estimated creatinine clearance. Reduce or withhold dose as appropriate.

Tumor Lysis Syndrome

- Cases of Tumor Lysis Syndrome (TLS), including fatal outcomes, have occurred in patients receiving KYPROLIS. Patients with multiple myeloma and a high tumor burden should be considered at greater risk for TLS. Adequate hydration is required prior to each dose in Cycle 1, and in subsequent cycles as needed. Consider uric acid lowering drugs in patients at risk for TLS. Monitor for evidence of TLS during treatment and manage promptly. Withhold KYPROLIS until TLS is resolved.

Pulmonary Toxicity

- Acute Respiratory Distress Syndrome (ARDS), acute respiratory failure, and acute diffuse infiltrative pulmonary disease such as pneumonitis and interstitial lung disease have occurred in patients receiving KYPROLIS. Some events have been fatal. In the event of drug-induced pulmonary toxicity, discontinue KYPROLIS.

Pulmonary Hypertension

- Pulmonary arterial hypertension (PAH) was reported in patients treated with KYPROLIS. Evaluate with cardiac imaging and/or other tests as indicated. Withhold KYPROLIS for PAH until resolved or returned to baseline and consider whether to restart KYPROLIS based on a benefit/risk assessment.

Dyspnea

- Dyspnea was reported in patients treated with KYPROLIS. Evaluate dyspnea to exclude cardiopulmonary conditions including cardiac failure and pulmonary syndromes. Stop KYPROLIS for Grade 3 or 4 dyspnea until resolved or returned to baseline. Consider whether to restart KYPROLIS based on a benefit/risk assessment.

Hypertension

- Hypertension, including hypertensive crisis and hypertensive emergency, has been observed with KYPROLIS. Some of these events have been fatal. Monitor blood pressure regularly in all patients. If hypertension cannot be adequately controlled, withhold KYPROLIS and evaluate. Consider whether to restart KYPROLIS based on a benefit/risk assessment.

Venous Thrombosis

- Venous thromboembolic events (including deep venous thrombosis and pulmonary embolism) have been observed with KYPROLIS. Thromboprophylaxis is recommended for patients being treated with the combination of KYPROLIS with dexamethasone or with lenalidomide plus dexamethasone. The thromboprophylaxis regimen should be based on an assessment of the patient's underlying risks.
- Patients using oral contraceptives or a hormonal method of contraception associated with a risk of thrombosis should consider an alternative method of effective contraception during treatment with KYPROLIS in combination with dexamethasone or lenalidomide plus dexamethasone.

Infusion Reactions

- Infusion reactions, including life-threatening reactions, have occurred in patients receiving KYPROLIS. Symptoms include fever, chills, arthralgia, myalgia, facial flushing, facial edema, vomiting, weakness, shortness of breath, hypotension, syncope, chest tightness, or angina. These reactions can occur immediately following or up to 24 hours after administration of KYPROLIS. Premedicate with dexamethasone to reduce the incidence and severity of infusion reactions. Inform patients

of the risk and of symptoms of an infusion reaction and to contact a physician immediately if they occur.

Thrombocytopenia

- KYPROLIS causes thrombocytopenia with recovery to baseline platelet count usually by the start of the next cycle. Thrombocytopenia was reported in patients receiving KYPROLIS. Monitor platelet counts frequently during treatment with KYPROLIS. Reduce or withhold dose as appropriate.

Hepatic Toxicity and Hepatic Failure

- Cases of hepatic failure, including fatal cases, have been reported during treatment with KYPROLIS. KYPROLIS can cause increased serum transaminases. Monitor liver enzymes regularly regardless of baseline values. Reduce or withhold dose as appropriate.

Thrombotic Microangiopathy

- Cases of thrombotic microangiopathy, including thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS), including fatal outcome have occurred in patients receiving KYPROLIS. Monitor for signs and symptoms of TTP/HUS. Discontinue KYPROLIS if diagnosis is suspected. If the diagnosis of TTP/HUS is excluded, KYPROLIS may be restarted. The safety of reinitiating KYPROLIS therapy in patients previously experiencing TTP/HUS is not known.

Posterior Reversible Encephalopathy Syndrome (PRES)

- Cases of PRES have occurred in patients receiving KYPROLIS. PRES was formerly known as Reversible Posterior Leukoencephalopathy Syndrome. Consider a neuroradiological imaging (MRI) for onset of visual or neurological symptoms. Discontinue KYPROLIS if PRES is suspected and evaluate. The safety of reinitiating KYPROLIS therapy in patients previously experiencing PRES is not known.

Embryo-fetal Toxicity

- KYPROLIS can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings in animals.
- Females of reproductive potential should be advised to avoid becoming pregnant while being treated with KYPROLIS. Males of reproductive potential should be advised to avoid fathering a child while being treated with KYPROLIS. If this drug is used during pregnancy, or if pregnancy occurs while taking this drug, the patient should be apprised of the potential hazard to the fetus.

ADVERSE REACTIONS

- The most common adverse events occurring in at least 20% of patients treated with KYPROLIS in the combination therapy trials: anemia, neutropenia, diarrhea, dyspnea, fatigue, thrombocytopenia, pyrexia, insomnia, muscle spasm, cough, upper respiratory tract infection, hypokalemia.
- The most common adverse events occurring in at least 20% of patients treated with KYPROLIS in monotherapy trials: anemia, fatigue, thrombocytopenia, nausea, pyrexia, dyspnea, diarrhea, headache, cough, edema peripheral.

Please see full Prescribing Information at www.kyprolis.com.

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) 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 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 (e.g., 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 ir patients who have underlying autoimmune disease or before continuing treatment in patients who develop immune-mediated events.
- **Plasmacytoma at 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.

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 full Prescribing Information and Medication Guide for IMLYGIC™ at www.IMLYGIC.com.

About Vectibix® (panitumumab)
Vectibix is the first fully human monoclonal anti-epidermal growth factor receptor (EGFR) antibody approved by the FDA for the treatment of metastatic colorectal cancer (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.

Important U.S. Product Information
Vectibix® is indicated for the treatment of patients with wild-type *KRAS* (exon 2 in codons 12 or 13) metastatic colorectal cancer (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

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

WARNING: DERMATOLOGIC TOXICITY
Dermatologic Toxicity: Dermatologic toxicities occurred in 90 percent of patients and were severe (NCI-CTC grade 3 or higher) in 15% of patients receiving Vectibix monotherapy.

In Study 1, 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 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 (e.g., 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 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 3, 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 2) 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 1, 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 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.

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.

Advise patients of the need for adequate contraception in both males and females while receiving Vectibix® and for 6 months after the last dose of Vectibix® therapy. Vectibix® may be transmitted from the mother to the developing fetus, and has the potential to cause fetal harm when administered to pregnant women.

Because many drugs are excreted into human milk and because of the potential for serious adverse reactions in nursing infants from Vectibix®, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. If nursing is interrupted, it should not be resumed earlier than 2 months following the last dose of Vectibix®.

Women who become pregnant during Vectibix® treatment are encouraged to enroll in Amgen's Pregnancy Surveillance Program. Women who are nursing during Vectibix® treatment are encouraged to enroll in Amgen's Lactation Surveillance Program. Patients or their physicians should call 1-800-77-AMGEN (1-800-772-6436) to enroll.

In Study 1, the most common adverse reactions (≥ 20%) with Vectibix® were skin rash with variable presentations, paronychia, fatigue, nausea, and diarrhea. The most common (> 5%) serious adverse reactions in the Vectibix® arm were general physical health deterioration and intestinal obstruction.

In Study 3, 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) 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 Vectibix® Prescribing Information, including Boxed Warning visit www.vectibix.com.

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 and FOLFIRI.
- 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.

About Neulasta® (pegfilgrastim)
Neulasta is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia. Neulasta is not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation.

In a pivotal clinical trial, in patients with nonmyeloid malignancies undergoing myelosuppressive chemotherapy associated with a clinically significant incidence of febrile neutropenia, treatment with Neulasta was shown to significantly reduce the incidence of febrile neutropenia..

Neulasta is administered by manual injection and is also available via the Neulasta® Onpro™ kit, which was approved by the FDA in 2014 and includes a specially designed, single-use prefilled syringe co-packaged with an on-body injector for Neulasta.
For more information about Neulasta, visit www.Neulasta.com and www.NeulastaHCP.com.

Important Safety Information Regarding Neulasta®

Contraindication
Do not administer Neulasta® to patients with a history of serious allergic reactions to pegfilgrastim or filgrastim.

Splenic Rupture
Splenic rupture, including fatal cases, can occur following the administration of Neulasta®. Evaluate for an enlarged spleen or splenic rupture in patients who report left upper abdominal or shoulder pain after receiving Neulasta®.

Acute Respiratory Distress Syndrome
Acute respiratory distress syndrome (ARDS) can occur in patients receiving Neulasta®. Evaluate patients who develop fever and lung infiltrates or respiratory distress after receiving Neulasta for ARDS. Discontinue Neulasta® in patients with ARDS.

Serious Allergic Reactions

Serious allergic reactions, including anaphylaxis, can occur in patients receiving Neulasta®. The majority of reported events occurred upon initial exposure. Allergic reactions, including anaphylaxis, can recur within days after the discontinuation of initial anti-allergic treatment. Permanently discontinue Neulasta® in patients with serious allergic reactions.

Allergies to Acrylics
The on-body injector for Neulasta® uses acrylic adhesive. For patients who have reactions to acrylic adhesives, use of this product may result in a significant reaction.

Use in Patients with Sickle Cell Disorders
Severe sickle cell crises can occur in patients with sickle cell disorders receiving Neulasta®. Severe and sometimes fatal sickle cell crises can occur in patients with sickle cell disorders receiving filgrastim, the parent compound of pegfilgrastim.

Glomerulonephritis
Glomerulonephritis has been reported in patients receiving Neulasta®. The diagnoses were based upon azotemia, hematuria (microscopic and macroscopic), proteinuria, and renal biopsy. Generally, events of glomerulonephritis resolved after withdrawal of Neulasta®. If glomerulonephritis is suspected, evaluate for cause. If causality is likely, consider dose-reduction or interruption of Neulasta®.

Leukocytosis
White blood cell counts of 100 x 109/L or greater have been observed in patients receiving pegfilgrastim. Monitoring of CBCs during pegfilgrastim therapy is recommended.

Capillary Leak Syndrome
Capillary leak syndrome has been reported after granulocyte colony-stimulating factor (G-CSF) administration, including Neulasta®, and is characterized by hypotension, hypoalbuminemia, edema, and hemoconcentration. Episodes vary in frequency, severity and may be life-threatening if treatment is delayed. Patients who develop symptoms of capillary leak syndrome should be closely monitored and receive standard symptomatic treatment, which may include a need for intensive care.

Potential for Tumor Growth Stimulatory Effects on Malignant Cells
The granulocyte colony-stimulating factor (G-CSF) receptor, through which pegfilgrastim and filgrastim act, has been found on tumor cell lines. The possibility that pegfilgrastim acts as a growth factor for any tumor type, including myeloid malignancies and myelodysplasia, diseases for which pegfilgrastim is not approved, cannot be excluded.

The most common adverse reactions (≥ 5% difference in incidence) in placebo-controlled clinical trials are bone pain and pain in extremity.

Please see additional Neulasta® Safety Information, by visiting www.amgen.com/medpro/products.html.

Please see the Neulasta Full Prescribing Information by clicking here.

About ABP 215
ABP 215 is being developed as a biosimilar to bevacizumab, which is approved in specific combinations in the U.S., EU and other regions for the treatment of patients with unresectable, locally advanced, recurrent or metastatic non-squamous NSCLC as well as metastatic carcinoma of the colon or rectum; metastatic renal cell carcinoma; and other region-specific indications.

About the Amgen and Allergan Collaboration
In December 2011, Amgen and Allergan plc. (then Watson Pharmaceuticals, Inc.) formed a collaboration to develop and commercialize, on a worldwide basis, four oncology antibody biosimilar medicines. This collaboration reflects the shared belief that the development and commercialization of biosimilar products will not follow a pure brand or generic model, and will require significant expertise, infrastructure, and investment to ensure safe, reliably supplied therapies for patients. Under the terms of the agreement, Amgen will assume primary responsibility for developing, manufacturing and initially commercializing the oncology antibody products.

About Amgen Biosimilars
Amgen Biosimilars is committed to building upon Amgen's experience in the development and manufacturing of innovative human therapeutics to expand Amgen's reach to patients suffering from serious illnesses. Biosimilars offer the potential to increase patient access to vital medicines, and Amgen is well positioned to leverage its 35 years of experience in biotechnology to create high-quality biosimilars and reliably supply them to patients worldwide.

For more information, visit www.amgenbiosimilars.com and follow us www.twitter.com/amgenbiosim.

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 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.

About Amgen's Commitment to Oncology
Amgen Oncology is committed to helping patients take on some of the toughest cancers, such as those that have been resistant to drugs, those that progress rapidly through the body and those where limited treatment options exist. Amgen's supportive care treatments help patients combat certain side effects of strong chemotherapy, and our targeted medicines and immunotherapies focus on more than a dozen different malignancies, ranging from blood cancers to solid tumors. With decades of experience providing therapies for cancer patients, Amgen continues to grow its portfolio of innovative and biosimilar oncology medicines.

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 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 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. 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. 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 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. 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. 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. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all. We are increasingly dependent on information technology systems, infrastructure and data security. 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.

The scientific information discussed in this news release related to our product candidates is preliminary and investigative. Such product candidates are not approved by the U.S. Food and Drug Administration, and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidates. Further, 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 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.

CONTACT: Amgen, Thousand Oaks
Kristen Davis, 805-447-3008 (Media)
Kristen Neese, 805-313-8267 (Media)
Arvind Sood, 805-447-1060 (Investors)

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