Amgen Data At ASCO 2015 Highlight Oncology Pipeline And Portfolio

May 13, 2015

THOUSAND OAKS, Calif., May 13, 2015 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced that data at the 51st Annual Meeting of the American Society of Clinical Oncology (ASCO) will showcase the Company's continued efforts across both pipeline and marketed products, including key results in the treatment of solid tumors and hematologic malignancies.

"The data at ASCO reflect our significant progress in developing treatments across our oncology pipeline and portfolio," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "Our focus is to address unmet needs for patients by translating innovation in research into much-needed therapeutic options."

Key data include new findings from clinical trials in multiple myeloma, breast cancer, metastatic melanoma, acute lymphoblastic leukemia (ALL) and metastatic colorectal cancer (mCRC).

Latest Research in Hematologic Malignancies:

Kyprolis ® (carfilzomib) for Injection
In multiple myeloma, full results are being presented from the Phase 3 head-to-head ENDEAVOR trial evaluating Kyprolis compared to Velcade® (bortezomib), as well as results from the Phase 1/2 CHAMPION-1 study and a secondary analysis from the pivotal Phase 3 ASPIRE study.

- **Carfilzomib and dexamethasone vs. bortezomib and dexamethasone in patients with relapsed multiple myeloma: results from the Phase 3 study ENDEAVOR**
  Abstract No. 8509, Lymphoma and Plasma Cell Disorders Oral Abstract Session, Tuesday, June 2, 9:45 a.m. to 12:45 p.m. CT (Presentation Time: 9:57 a.m. to 10:09 a.m. CT), E354b
- **Updated results from CHAMPION-1, a Phase 1/2 study investigating weekly carfilzomib with dexamethasone for patients with relapsed or refractory multiple myeloma**
  Abstract No. 8527, Lymphoma and Plasma Cell Disorders Poster Session, Sunday, May 31, 8 a.m. to 11:30 a.m. CT, S Hall A
- **Effect of carfilzomib, lenalidomide, and dexamethasone vs. lenalidomide and dexamethasone in patients with relapsed multiple myeloma by line of therapy: secondary analysis from an interim analysis of the Phase 3 study ASPIRE**
  Abstract No. 8525, Lymphoma and Plasma Cell Disorders Poster Session, Sunday, May 31, 8 a.m. to 11:30 a.m. CT, S Hall A

BLINCYTO® (blinatumomab)
BLINCYTO data at ASCO will focus on targeted patient populations within adult relapsed/refractory ALL to better understand response to treatment.

- **Re-exposure to blinatumomab after CD19-positive relapse: Experience from three trials in patients with relapsed/refractory B-precursor acute lymphoblastic leukemia**
  Abstract No. 7051, Leukemia, Myelodysplasia, and Transplantation Poster Session, Sunday, May 31, 8 a.m. to 11:30 a.m. CT, S Hall A
- **Safety and activity of blinatumomab for older patients with relapsed/refractory B-precursor acute lymphoblastic leukemia in two Phase 2 studies**
  Abstract No. 7043, Leukemia, Myelodysplasia, and Transplantation Poster Session, Sunday, May 31, 8 a.m. to 11:30 a.m. CT, S Hall A
- **Factors influencing outcomes in patients with relapsed/refractory B-precursor acute lymphoblastic leukemia treated with blinatumomab in a Phase 2 study**
  Abstract No. 7057, Leukemia, Myelodysplasia, and Transplantation Poster Session, Sunday, May 31, 8 a.m. to 11:30 a.m. CT, S Hall A
- **Pharmacokinetics/pharmacodynamics of blinatumomab in patients with relapsed/refractory B-precursor acute lymphoblastic leukemia**
  Abstract No. 2561, Developmental Therapeutics Poster Session, Saturday, May 30, 8 a.m. to 11:30 a.m. CT, S Hall A

Key Data in Solid Tumors and Supportive Care:

Prolia® (denosumab)
Results will be featured from a Phase 3 study evaluating the effects of denosumab compared with placebo on time to first clinical fracture in postmenopausal patients with hormone receptor positive breast cancer receiving aromatase inhibitor (AI) treatment.

- **Adjuvant denosumab in breast cancer: results from 3,425 postmenopausal patients of the ABCSG-18 trial**
  Abstract No. 504, Breast Cancer Oral Abstract Session, Monday, June 1, 8 a.m. to 11 a.m. CT (Presentation Time: 9:12

a.m. to 9:24 a.m. CT), N Hall B1

Talimogene Laherparepvec
New talimogene laherparepvec data will be presented from combination studies with checkpoint inhibitors (anti-PD1 and anti-CTLA4), a neoadjuvant trial in progress, and additional analyses from the pivotal Phase 3 OPTiM study in patients with metastatic melanoma.

- **Survival, safety, and response patterns in a Phase 1b multicenter trial of talimogene laherparepvec and ipilimumab in previously untreated, unresected stage IIIB-IV melanoma**
  Abstract No. 9063, Melanoma/Skin Cancers Poster Session, Monday, June 1, 1:15 p.m. to 4:45 p.m. CT, S Hall A
- **Tumor size and clinical outcomes in melanoma patients treated with talimogene laherparepvec**
  Abstract No. 9074, Melanoma/Skin Cancers Poster Session, Monday, June 1, 1:15 p.m. to 4:45 p.m. CT, S Hall A
- **A multicenter, open-label trial of talimogene laherparepvec plus pembrolizumab vs. pembrolizumab monotherapy in previously untreated, unresected, stage IIIB-IV melanoma (Trials in Progress abstract)**
  Abstract No. TPS9081, Melanoma/Skin Cancers Poster Session, Monday, June 1, 1:15 p.m. to 4:45 p.m. CT, S Hall A
- **Phase 2, multicenter, randomized, open-label trial assessing efficacy and safety of talimogene laherparepvec neoadjuvant treatment plus surgery vs. surgery for resectable Stage IIIB/C and IVM1a melanoma (Trials in Progress abstract)**
  Abstract No. TPS9094, Melanoma/Skin Cancers Poster Session, Monday, June 1, 1:15 p.m. to 4:45 p.m. CT, S Hall A

Vectibix® (panitumumab)
In addition to final results from the Phase 3 ASPECCT study, which investigates Vectibix compared to cetuximab in wild-type *KRAS* mCRC, results from the Phase 2 PEAK study, the Phase 3 PRIME trial and the Phase 2 '314 study, which examines expression of amphiregulin and response to first-line Vectibix plus FOLFIRI, will be presented.

- **Final results from ASPECCT: Randomized Phase 3 non-inferiority study of panitumumab vs. cetuximab in chemorefractory wild-type KRAS exon 2 metastatic colorectal cancer**
  Abstract No. 3586, Gastrointestinal (Colorectal) Cancer Poster Session, Monday, June 1, 8 a.m. to 11:30 a.m. CT, S Hall A
- **Randomized Phase 3 study of panitumumab vs. cetuximab in chemorefractory wild-type KRAS exon 2 metastatic colorectal cancer: outcomes by hypomagnesemia in ASPECCT**
  Abstract No. 3587, Gastrointestinal (Colorectal) Cancer Poster Session, Monday, June 1, 8 a.m. to 11:30 a.m. CT, S Hall A
- **Tumor response outcomes in first-line treatment of wild-type RAS metastatic colorectal carcinoma following modified FOLFOX6 + either panitumumab or bevacizumab**
  Abstract No. 3535, Gastrointestinal (Colorectal) Cancer Poster Session, Monday, June 1, 8 a.m. to 11:30 a.m. CT, S Hall A
- **The PRIME trial: Quality-adjusted survival in patients with RAS wild-type metastatic colorectal cancer receiving first-line therapy with panitumumab plus FOLFOX vs. FOLFOX alone**
  Abstract No. 3543, Gastrointestinal (Colorectal) Cancer Poster Session, Monday, June 1, 8 a.m. to 11:30 a.m. CT, S Hall A
- **Expression of amphiregulin and response to first-line panitumumab + FOLFIRI in metastatic colorectal cancer**
  Abstract No. 3536, Gastrointestinal (Colorectal) Cancer Poster Session, Monday, June 1, 8 a.m. to 11:30 a.m. CT, S Hall A

Neulasta® (pegfilgrastim)
Results from three studies evaluating the impact of administration and the risk of febrile neutropenia following myelosuppresive chemotherapy administration will be published.

- **Risk of febrile neutropenia in cancer patients receiving myelosuppressive chemotherapy and pegfilgrastim prophylaxis: does day of administration matter? (Publication Only abstract)**
- **Risk of chemotherapy-induced febrile neutropenia with early discontinuation of pegfilgrastim prophylaxis in U.S. clinical practice (Publication Only abstract)**
- **Effect of timing of pegfilgrastim administration on absolute neutrophil count trajectory among cancer patients receiving myelosuppressive chemotherapy (Publication Only abstract)**

XGEVA® (denosumab)
An ongoing head-to-head clinical trial investigating XGEVA compared to zoledronic acid in patients with multiple myeloma will be presented (study 20090482).

- **Denosumab compared with zoledronic acid for the treatment of bone disease in adults with newly diagnosed multiple myeloma; An international, randomized, double-blind trial (Trial in Progress Abstract)**
  Abstract No. TPS8611, Lymphoma and Plasma Cell Disorders Poster Session, Sunday, May 31, 8 a.m. to 11:30 a.m. CT, S Hall A

Amgen Post-ASCO Summary Webcast
Amgen will hold a post-ASCO summary webcast on Tuesday, June 2 at 1 p.m. CT. Sean E. Harper, M.D., executive vice president of Research and Development at Amgen, along with members of Amgen's clinical development team and clinical investigators will participate to discuss data presented at ASCO and Amgen's broader oncology portfolio of products.

Live audio of the event will be simultaneously broadcast over the Internet and will be available to members of the news media, investors and the

general public.

The webcast, as with other selected presentations regarding developments in Amgen's business given by management at certain investor and medical conferences, can be found on Amgen's website, www.amgen.com, under Investors. Information regarding presentation times, webcast availability and webcast links are noted on Amgen's Investor Relations Events Calendar. The webcast will be archived and available for replay for at least 90 days after the event.

About Kyprolis® (carfilzomib) for Injection
On July 20, 2012, the U.S. FDA granted accelerated approval of Kyprolis for the treatment of patients with multiple myeloma who have received at least two prior therapies including bortezomib and an immunomodulatory agent (IMiD) and have demonstrated disease progression on or within 60 days of completion of the last therapy. Approval was based on response rate. Clinical benefit, such as improvement in survival or symptoms, has not been verified.

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. Kyprolis is also approved for use in Argentina, Israel and Mexico. For more information about Kyprolis, visit www.kyprolis.com.

Important Safety Information Regarding Kyprolis® (carfilzomib) for Injection
This safety information is specific to the current U.S. approved indication, which is based on Phase 2 studies.

Safety data have been evaluated in 526 patients with relapsed and/or refractory multiple myeloma who received single-agent Kyprolis. There were 37 deaths in the Phase 2 studies, or 7 percent of patients. The most common causes of death, other than disease progression, were cardiac events (5 patients), end-organ failure (4 patients) and infection (4 patients). Important warnings and precautions include cardiac arrest, congestive heart failure, myocardial ischemia, pulmonary hypertension, pulmonary complications, infusion reactions, tumor lysis syndrome, thrombocytopenia, hepatic toxicity, thrombotic thrombocytopenic purpura / hemolytic uremic syndrome (TTP/HUS), posterior reversible encephalopathy syndrome (PRES), and embryo-fetal toxicity.

Death due to cardiac arrest has occurred within a day of Kyprolis administration. Patients with New York Heart Association Class III and IV heart failure, myocardial infarction in the preceding 6 months and conduction abnormalities uncontrolled by medications were not eligible for the clinical trials. These patients may be at greater risk for cardiac complications.

Pulmonary arterial hypertension (PAH) was reported in 2 percent of patients treated with Kyprolis and was Grade 3 or greater in less than 1 percent of patients. Dyspnea was reported in 35 percent of patients enrolled in clinical trials. Grade 3 dyspnea occurred in 5 percent; no Grade 4 events and 1 death (Grade 5) was reported.

Infusion reactions, characterized by a spectrum of systemic symptoms including fever, chills, arthralgia, myalgia, facial flushing, facial edema, vomiting, weakness, shortness of breath, hypotension, syncope, chest tightness, or angina can occur immediately following or up to 24 hours after administration of Kyprolis. Administration of dexamethasone prior to Kyprolis reduces the incidence and severity of reactions. Tumor lysis syndrome (TLS) occurred following Kyprolis administration in <1 percent of patients. Patients with multiple myeloma and a high tumor burden should be considered to be at greater risk for TLS.

Thrombocytopenia following Kyprolis administration resulted in a dose reduction in 1 percent of patients and discontinuation of treatment with Kyprolis in <1 percent of patients.

Cases of hepatic failure, including fatal cases, have been reported (<1 percent). Kyprolis can cause elevations of serum transaminases and bilirubin.

Cases of thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS) including fatal outcome have been reported in patients who received KYPROLIS.

PRES, formerly termed Reversible Posterior Leukoencephalopathy Syndrome (RPLS), is a neurological disorder, which can present with seizure, headache, lethargy, confusion, blindness, altered consciousness, and other visual and neurological disturbances, along with hypertension, and the diagnosis is confirmed by neuro-radiological imaging (MRI). Cases of PRES have been reported in patients receiving KYPROLIS.

There are no adequate and well-controlled studies in pregnant women using Kyprolis. Females of reproductive potential should be advised to avoid becoming pregnant while being treated with Kyprolis.

The most common serious adverse reactions were pneumonia, acute renal failure, pyrexia and congestive heart failure. The most common adverse reactions (incidence of 30 percent or greater) observed in clinical trials of patients with multiple myeloma were fatigue, anemia, nausea, thrombocytopenia, dyspnea, diarrhea and pyrexia. Serious adverse reactions were reported in 45 percent of patients.

Full prescribing information is available at www.kyprolis.com.

About BLINCYTO® (blinatumomab)
BLINCYTO is first FDA-approved bispecific CD19-directed CD3 T-cell engager (BiTE®) antibody construct product, and the first single-agent immunotherapy to be approved for the treatment of patients with Philadelphia chromosome-negative relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL). Prior to approval, BLINCYTO was granted breakthrough therapy and priority review designation by the FDA.

Important U.S. Product Information
BLINCYTO is indicated for the treatment of Philadelphia chromosome-negative relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

This indication is approved under accelerated approval. Continued approval for this indication may be contingent upon verification of clinical benefit in subsequent trials.

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGICAL TOXICITIES

- **Cytokine Release Syndrome (CRS), which may be life-threatening or fatal, occurred in patients receiving BLINCYTO. Interrupt or discontinue BLINCYTO as recommended.**
- **Neurological toxicities, which may be severe, life-threatening or fatal, occurred in patients receiving BLINCYTO. Interrupt or discontinue BLINCYTO as recommended.**

Contraindications
BLINCYTO is contraindicated in patients with a known hypersensitivity to blinatumomab or to any component of the product formulation.

Warnings and Precautions

- Cytokine Release Syndrome (CRS): Life-threatening or fatal CRS occurred in patients receiving BLINCYTO. Infusion reactions have occurred and may be clinically indistinguishable from manifestations of CRS. Closely monitor patients for signs and symptoms of serious events such as pyrexia, headache, nausea, asthenia, hypotension, increased alanine aminotransferase (ALT), increased aspartate aminotransferase (AST), increased total bilirubin (TBILI), disseminated intravascular coagulation (DIC), capillary leak syndrome (CLS), and hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS). Interrupt or discontinue BLINCYTO as outlined in the Prescribing Information (PI).
- Neurological Toxicities: Approximately 50% of patients receiving BLINCYTO in clinical trials experienced neurological toxicities. Severe, life-threatening, or fatal neurological toxicities occurred in approximately 15% of patients, including encephalopathy, convulsions, speech disorders, disturbances in consciousness, confusion and disorientation, and coordination and balance disorders. The median time to onset of any neurological toxicity was 7 days. Monitor patients for signs or symptoms and interrupt or discontinue BLINCYTO as outlined in the PI.
- Infections: Approximately 25% of patients receiving BLINCYTO experienced serious infections, some of which were life-threatening or fatal. Administer prophylactic antibiotics and employ surveillance testing as appropriate during treatment. Monitor patients for signs or symptoms of infection and treat appropriately, including interruption or discontinuation of BLINCYTO as needed.
- Tumor Lysis Syndrome (TLS): Life-threatening or fatal TLS has been observed. Preventive measures, including pretreatment nontoxic cytoreduction and on treatment hydration, should be used during BLINCYTO treatment. Monitor patients for signs and symptoms of TLS and interrupt or discontinue BLINCYTO as needed to manage these events.
- Neutropenia and Febrile Neutropenia, including life-threatening cases, have been observed. Monitor appropriate laboratory parameters during BLINCYTO infusion and interrupt BLINCYTO if prolonged neutropenia occurs.
- Effects on Ability to Drive and Use Machines: Due to the possibility of neurological events, including seizures, patients receiving BLINCYTO® are at risk for loss of consciousness, and should be advised against driving and engaging in hazardous occupations or activities such as operating heavy or potentially dangerous machinery while BLINCYTO® is being administered.
- Elevated Liver Enzymes: Transient elevations in liver enzymes are associated with BLINCYTO® treatment. The majority of these events were observed in the setting of CRS. The median time to onset was 15 days. Grade 3 or greater elevations in liver enzymes occurred in 6% of patients outside the setting of CRS and resulted in treatment discontinuation in less than 1% of patients. Monitor ALT, AST, gamma-glutamyl transferase (GGT), and TBILI prior to the start of and during BLINCYTO® treatment. BLINCYTO treatment should be interrupted if transaminases rise to > 5 times the upper limit of normal (ULN) or if TBILI rises to > 3 times ULN.
- Leukoencephalopathy: Although the clinical significance is unknown, cranial magnetic resonance imaging (MRI) changes showing leukoencephalopathy have been observed in patients receiving BLINCYTO®, especially in patients previously treated with cranial irradiation and anti-leukemic chemotherapy.
- Preparation and administration errors have occurred. Follow instructions for preparation (including admixing) and administration in the PI strictly to minimize medication errors (including underdose and overdose).

Adverse Events
The most commonly reported adverse reactions (≥ 20%) in clinical trials were pyrexia (62%), headache (36%), peripheral edema (25%), febrile neutropenia (25%), nausea (25%), hypokalemia (23%), rash (21%), tremor (20%) and constipation (20%).

Dosage and Administration Guidelines

- BLINCYTO is administered as a continuous intravenous infusion at a constant flow rate using an infusion pump which should be programmable, lockable, non-elastomeric, and have an alarm.
- It is very important that the instructions for preparation (including admixing) and administration provided in the full Prescribing Information are strictly followed to minimize medication errors (including underdose and overdose).

Please see full Prescribing Information and medication guide for BLINCYTO® at www.BLINCYTO.com.

About Prolia® (denosumab)
Prolia is the first approved therapy that specifically targets RANK Ligand, an essential regulator of bone-removing cells (osteoclasts).

Prolia is approved in the U.S. for the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy. Prolia is also approved for treatment to increase bone mass in men with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy.

Prolia is approved in the EU plus Switzerland, Norway, Iceland and Liechtenstein for the treatment of osteoporosis in postmenopausal women and in men at increased risk of fractures. Prolia is also approved in the EU for the treatment of bone loss associated with hormone ablation in men with prostate cancer at increased risk of fractures.

Prolia is also indicated as a treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer and in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer.

Prolia is administered as a single subcutaneous injection of 60 mg once every six months. Please see the Important Saftey Information below.

Important Safety Information (U.S.)
Prolia is contraindicated in patients with hypocalcemia. Preexisting hypocalcemia must be corrected prior to initiating Prolia. Prolia is contraindicated in women who are pregnant and may cause fetal harm. Prolia is contraindicated in patients with a history of systemic hypersensitivity to any component of the product. Reactions have included anaphylaxis, facial swelling and urticaria. Prolia contains the same active ingredient (denosumab) found in XGEVA®. Patients receiving Prolia should not receive XGEVA.

Clinically significant hypersensitivity including anaphylaxis has been reported with Prolia. Symptoms have included hypotension, dyspnea, throat tightness, facial and upper airway edema, pruritus, and urticaria. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue further use of Prolia. Hypocalcemia may worsen in patients taking Prolia, especially in patients with severe renal impairment. In patients predisposed to hypocalcemia and disturbances of mineral metabolism, clinical monitoring of calcium and mineral levels is highly recommended within 14 days of Prolia injection. Adequately supplement all patients with calcium and vitamin D.

Osteonecrosis of the jaw (ONJ), which can occur spontaneously, is generally associated with tooth extraction and/or local infection with delayed healing and has been reported in patients receiving Prolia. A routine oral exam should be performed by the prescriber prior to initiation of Prolia. A dental examination with appropriate preventive dentistry is recommended prior to treatment with Prolia in patients with risk factors for ONJ such as invasive dental procedures, diagnosis of cancer, concomitant therapies (e.g., chemotherapy, corticosteroids, angiogenesis inhibitors), poor oral hygiene, and co-morbid disorders. Good oral hygiene practices should be maintained during treatment. For patients requiring invasive dental procedures, clinical judgment should guide the management plan of each patient. Patients who are suspected of having or who develop ONJ should receive care by a dentist or an oral surgeon. Extensive dental surgery to treat ONJ may exacerbate the condition. Discontinuation of Prolia therapy should be considered based on individual benefit-risk assessment.

Atypical low-energy or low trauma fractures of the shaft have been reported in patients receiving Prolia. Causality has not been established as these fractures also occur in osteoporotic patients who have not been treated with antiresorptive agents. During Prolia 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 evaluated to rule out an incomplete femur fracture. Interruption of Prolia therapy should be considered, pending a risk/benefit assessment, on an individual basis.

In a clinical trial (N= 7800) in women with postmenopausal osteoporosis, serious infections leading to hospitalization were reported more frequently in the Prolia group than in the placebo group. Serious skin infections, as well as infections of the abdomen, urinary tract and ear were more frequent in patients treated with Prolia. Endocarditis was also reported more frequently in Prolia-treated patients. The incidence of opportunistic infections and the overall incidence of infections were similar between the treatment groups. Advise patients to seek prompt medical attention if they develop signs or symptoms of severe infection, including cellulitis. Patients on concomitant immunosuppressant agents or with impaired immune systems may be at increased risk for serious infections. In patients who develop serious infections while on Prolia, prescribers should assess the need for continued Prolia therapy.

In the same clinical trial in women with postmenopausal osteoporosis, epidermal and dermal adverse events such as dermatitis, eczema and rashes occurred at a significantly higher rate with Prolia compared to placebo. Most of these events were not specific to the injection site. Consider discontinuing Prolia if severe symptoms develop.

Severe and occasionally incapacitating bone, joint, and/or muscle pain has been reported in patients taking Prolia. Consider discontinuing use if severe symptoms develop. Suppression of Bone Turnover In clinical trials in women with postmenopausal osteoporosis, Prolia resulted in significant suppression of bone remodeling as evidenced by markers of bone turnover and bone histomorphometry. The significance of these findings and the effect of long-term treatment are unknown. Monitor patients for these consequences, including ONJ, atypical fractures, and delayed fracture healing.

It is not known whether Prolia is excreted into human milk. Measurable concentrations of denosumab were present in the maternal milk of cynomolgus monkeys up to 1 month after the last dose of denosumab (≤ 0.5% milk:serum ratio). Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Prolia®, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

The most common adverse reactions (>5% and more common than placebo) in women with postmenopausal osteoporosis are back pain, pain in extremity, musculoskeletal pain, hypercholesterolemia, and cystitis. The most common adverse reactions (> 5% and more common than placebo) in men with osteoporosis are back pain, arthralgia, and nasopharyngitis. Pancreatitis has been reported with Prolia. In women with postmenopausal osteoporosis, the overall incidence of new malignancies was 4.3% in the placebo group and 4.8% in the Prolia groups. In men with osteoporosis, new malignancies were reported in no patients in the placebo group and 4 (3.3%) patients in the Prolia group. A causal relationship to drug exposure has not been established. Denosumab is a human monoclonal antibody. As with all therapeutic proteins, there is potential for immunogenicity. The most common (per patient incidence ≥ 10%) adverse reactions reported with Prolia in patients with bone loss receiving ADT for prostate cancer or adjuvant AI therapy for breast cancer are arthralgia and back pain. Pain in extremity and musculoskeletal pain have also been reported in clinical trials. Additionally, in Proliatreated men with nonmetastatic prostate cancer receiving ADT, a greater incidence of cataracts was observed.

For more information, please see the Prolia Important Safety Information, Prescribing Information, and Medication Guide.

The Prolia Postmarketing Active Safety Surveillance Program is available to collect information from prescribers on specific adverse events. Please

see www.proliasafety.com or call 18007726436 for more information

About Talimogene Laherparepvec
Talimogene laherparepvec is an investigational oncolytic immunotherapy designed to selectively replicate in tumors (but not normal tissue) and to initiate an immune response to target cancer cells that have metastasized. Talimogene laherparepvec was designed to work in two important and complementary ways. First, it is injected directly into tumors where it replicates inside the tumor's cells causing the cell to rupture and die in a process called lysis. The rupture of the cancer cells can release tumor-derived antigens, along with GM-CSF, that can stimulate a system-wide immune response where white blood cells are able to seek out and target cancer that has spread throughout the body.

About Vectibix® (panitumumab)
Vectibix is a fully human anti-EGFR antibody. Vectibix is approved by the FDA for use in patients with wild-type *KRAS* (exon 2) mCRC in combination with FOLFOX as first-line treatment and as a monotherapy after disease progression after prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy. Vectibix is 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.

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.

In Study 1, 4% of patients experienced infusion reactions and 1% of patients experienced severe infusion reactions (NCI-CTC grade 3-4).

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.

Adverse Reactions
The most common adverse reactions (> 20%) of Vectibix are skin rash with variable presentations, paronychia, fatigue, nausea and diarrhea. The most frequently reported adverse reactions for Vectibix leading to withdrawal were general physical health deterioration and intestinal obstruction.

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) in Study 3 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 full Vectibix Safety Information, visit www.vectibix.com.

About Neulasta® (pegfilgrastim)
Neulasta is a leukocyte growth factor approved by the FDA in 2002, and is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anticancer 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 has been shown to significantly reduce the incidence of febrile neutropenia as well as hospitalizations related to febrile neutropenia and the use of IV antibiotics.[1]

For more information about Neulasta, visit www.Neulasta.com and www.NeulastaHCP.com.

Important Safety Information

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.

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 http://pi.amgen.com/united_states/neulasta/neulasta_pi_hcp_english.pdf.

About XGEVA® (denosumab)
XGEVA was approved by the FDA in 2010 for the prevention of skeletal-related events (SREs) in patients with bone metastases from solid tumors (XGEVA is not indicated for the prevention of SREs in patients with multiple myeloma).

In clinical trials, XGEVA demonstrated a clinically meaningful improvement compared to zoledronic acid (the previous standard of care) in preventing SREs, such as clinical fractures, surgery to the bone, spinal cord compression or radiation. XGEVA is administered as a single subcutaneous injection of 120 mg once every 4 weeks.

In 2013, XGEVA was approved by the FDA as the first-and-only treatment for 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.

In 2014, XGEVA was approved by the FDA for the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.

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 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.

Hypersensitivity
XGEVA is contraindicated in patients with known clinically significant hypersensitivity to XGEVA, including anaphylaxis that has been reported with use of XGEVA. 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) can occur in patients receiving XGEVA. 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. In clinical trials in patients with osseous metastasis, the incidence of ONJ was higher with longer duration of exposure.

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. During XGEVA treatment, patients should be advised

to report new or unusual thigh, hip, or groin pain. Patient 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.

Embryo-Fetal Toxicity
XGEVA can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use highly effective contraception during therapy, and for at least five months after the last dose of 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 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.

Denosumab is also marketed as Prolia® in other indications.

Please visit www.amgen.com or www.xgeva.com for Full Prescribing Information.

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 manufacturing 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 Inc. and its subsidiaries (Amgen, we or us) 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 Inc., including Amgen Inc.'s most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and Form 8-K. Please refer to Amgen Inc.'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 May 13, 2015, 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 and our partners 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 product liability claims. 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. 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 (including products of our wholly-owned subsidiaries) are affected by the 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 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 and our partners routinely obtain patents for our and their products and technology, the protection of our products offered by patents and patent applications may be challenged, invalidated or circumvented by our or our partners' competitors and there can be no guarantee of our or our partners' 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. Our efforts to integrate the operations of companies we have acquired may not be successful. We may experience difficulties, delays or unexpected costs and not achieve anticipated benefits and savings from our recently announced restructuring plan. 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 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 (FDA), 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 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.

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