



Amgen Highlights Key Clinical Data To Be Presented At European Cancer Congress 2015

September 14, 2015

Showcasing New Data in Solid Tumors and Supportive Care

THOUSAND OAKS, Calif., Sept. 14, 2015 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced it will present data from its oncology portfolio and pipeline at the European Cancer Congress 2015 (ECC 2015), Sept. 25 - 29, 2015, in Vienna.

"Amgen is excited to be sharing clinical data at ECC that demonstrates our commitment to advancing the scientific understanding of cancer care," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "Amgen's oncology research and development is focused on multiple pathways that may lead to deeper understanding of existing treatments and to the development of new treatment options for patients."

Key data to be presented at the congress include findings from clinical trials in melanoma, metastatic colorectal cancer and bone metastases.

Talimogene laherparepvec

Talimogene laherparepvec is an investigational oncolytic immunotherapy administered as an intralesional injection that is designed to initiate an anti-tumor immune response. Talimogene laherparepvec is under review by the European Medicines Agency and the U.S. Food and Drug Administration (FDA) for the treatment of metastatic melanoma. Data to be presented on talimogene laherparepvec will include:

- **Safety data from the Phase 1b part of the MASTERKEY-265 study combining talimogene laherparepvec (T-VEC) and pembrolizumab for unresectable stage IIIB-IV melanoma**
Abstract 24LBA, Oral Session, Sunday, Sept. 27, 11:30 a.m. – 12:30 p.m. CEST (Hall A2)
- **Durable complete responses (CR) in patients (pts) with stage IIIB-IV melanoma treated with talimogene laherparepvec (T-VEC) in OPTiM**
Abstract 3334 / P211, Poster Session, Sunday, Sept. 27, 4:45 p.m. – 6:45 p.m. CEST (Hall C)
- **Clinical benefits associated with durable response (DR) in patients (pts) with unresected stage IIIB/C/IV melanoma treated with talimogene laherparepvec (T-VEC) or GM-CSF in the randomized Phase 3 OPTiM trial (NCT00769704)**
Abstract 3330 / P207, Poster Session, Sunday, Sept. 27, 4:45 p.m. – 6:45 p.m. CEST (Hall C)

Vectibix® (panitumumab)

Vectibix, approved by the FDA and the European Commission for the treatment of metastatic colorectal cancer, is a fully human monoclonal antibody that targets epidermal growth factor receptor (EGFR), a protein that plays an important role in cancer cell signalling in many tumor types. Long-term survival data from the PEAK trial final analysis adds to the understanding of how Vectibix works when added to standard first-line chemotherapy for the treatment of wild-type *RAS* metastatic colorectal cancer. Overall, the Vectibix clinical trial program continues to generate additional data regarding biomarkers and drug sequencing. Data to be presented on Vectibix will include:

- **Final analysis of the PEAK trial: Overall survival (OS) and tumour responses during first-line treatment with mFOLFOX6 + either panitumumab (pmab) or bevacizumab (bev) in patients (pts) with metastatic colorectal carcinoma (mCRC)**
Abstract 2014, Poster Discussion, Sunday, Sept. 27, 8 a.m. – 9 a.m. CEST (Hall A1)
- **Efficacy outcomes by severity of skin toxicity from ASPECCT: Randomized Phase 3 study of panitumumab (pmab) versus cetuximab (cmab) in chemorefractory wild-type (WT) KRAS exon 2 metastatic colorectal cancer (mCRC)**
Abstract 2110 / P100, Poster Session, Sunday, Sept. 27, 9:15 a.m. – 11:15 a.m. CEST (Hall C)
- **Retrospective observational study to estimate the attrition of patients across lines of systemic treatment for metastatic colorectal cancer in Canada**
Abstract 2132 / P122, Poster Session, Sunday, Sept. 27, 9:15 a.m. – 11:15 a.m. CEST (Hall C)
- **Tumour response outcomes during the first-line treatment of metastatic colorectal carcinoma (mCRC) with panitumumab + FOLFIRI**
Abstract 2130 / P120, Poster Session, Sunday, Sept. 27, 9:15 a.m. – 11:15 a.m. CEST (Hall C)
- **Quality of life (QoL) during second-line treatment with FOLFIRI +/- panitumumab (pmab) in patients (pts) with RAS wild-type (WT) metastatic colorectal carcinoma (mCRC)**
Abstract 2118 / P108, Poster Session, Sunday, Sept. 27, 9:15 a.m. – 11:15 a.m. CEST (Hall C)
- **Highly sensitive and multiplexed next-generation sequencing MiSeqDx Extended RAS Panel for FFPE colorectal samples**
Abstract 803 / P146, Poster Session, Monday, Sept. 28, 4:45 p.m. – 6:45 p.m. CEST (Hall C)

XGEVA® (denosumab)

XGEVA, approved by the FDA and by the European Commission, targets the RANK ligand pathway to prevent the formation, function and survival of osteoclasts, which break down bone. XGEVA is indicated for the prevention of skeletal-related events (SREs) in patients with bone metastases from solid tumors and for treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity. SREs, also known as bone complications, are defined as radiation to bone, pathologic fracture, surgery to bone

and spinal cord compression. XGEVA is also indicated in the U.S. for the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.

Data to be presented at ECC may advance the understanding of XGEVA treatment for cancer patients who can be affected by the consequences of bone metastases. Data to be presented on XGEVA will include:

- **Incidence and proportion of bone metastases in women with breast cancer: A meta-analysis of the published literature**
Abstract 1029 / P148, Poster Session, Saturday, Sept. 26, 4:45 p.m. – 6:45 p.m. CEST (Hall C)
- **Prevalence of hypercalcemia of malignancy and associated survival in electronic health records (EHR) in the United States**
Abstract 1030 / P149, Poster Session, Saturday, Sept. 26, 4:45 p.m. – 6:45 p.m. CEST (Hall C)
- **Bone Targeting Agent (BTA) treatment patterns and the impact of bone metastases (BM) on prostate cancer patients in a real-world setting**
Abstract 1527 / P298, Poster Session, Sunday, Sept. 27, 4:45 p.m. – 6:45 p.m. CEST (Hall C)
- **Bone Targeting Agent (BTA) treatment patterns and the impact of bone metastases (BM) on advanced breast cancer patients in a real-world setting**
Abstract 1523 / P294, Poster Session, Sunday, Sept. 27, 4:45 p.m. – 6:45 p.m. CEST (Hall C)
- **An observational time and motion study of denosumab subcutaneous injection and zoledronic acid intravenous infusion in patients with metastatic bone disease: Results from Belgium and Germany**
Abstract 1617 / P388, Poster Session, Sunday, Sept. 27, 4:45 p.m. – 6:45 p.m. CEST (Hall C)
- **X-TREME: Interim analysis from a German open-label, observational study for treatment persistence with denosumab in routine use in adults with bone metastases secondary to solid tumours**
Abstract 1522 / P293, Poster Session, Sunday, Sept. 27, 4:45 p.m. – 6:45 p.m. CEST (Hall C)

Additional data from Neulasta[®] (pegfilgrastim), and AMG 337, an investigational, oral inhibitor of MET kinase activity, include:

- **Final results from PAVES, a Phase 3, randomized, double-blind, placebo-controlled trial of pegfilgrastim in patients receiving first-line FOLFOX or FOLFIRI and bevacizumab for locally advanced or metastatic colorectal cancer (LA/mCRC) (NCT00911170)**
Abstract 1609 / P380, Poster Session, Sunday, Sept. 27, 4:45 p.m. – 6:45 p.m. CEST (Hall C)
- **Evaluation of MET using FISH, IHC, or Mass Spectrometry as a prognostic biomarker in patients with gastroesophageal cancer**
Abstract 2397 / P359, Poster Session, Monday, Sept. 28, 9:15 a.m. – 11:15 a.m. CEST (Hall C)

Abstracts are available on the European Cancer Congress website at www.europeancancercongress.org/.

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 treatments for cancer patients, Amgen continues to grow its portfolio of innovative and biosimilar oncology medicines.

About Talimogene Laherparepvec

Talimogene laherparepvec is an investigational oncolytic immunotherapy designed to replicate in tumors 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 granulocyte-macrophage colony-stimulating factor (GM-CSF), that can stimulate an immune response where white blood cells are able to seek out and target cancer cells.

About Vectibix[®] (panitumumab)

In the European Union (EU), Vectibix is currently indicated for the treatment of adult patients with wild-type RAS mCRC:

- in first-line in combination with FOLFOX or 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.

Important EU Product Safety Information

Dermatologic related reactions, a pharmacologic effect observed with epidermal growth factor receptor (EGFR) inhibitors, are experienced with nearly all patients (approximately 90 percent) treated with Vectibix. The majority of dermatological reactions are mild to moderate in nature. In clinical studies, subsequent to the development of severe dermatological reactions (including stomatitis), infectious complications including sepsis, in rare cases leading to death, and local abscesses requiring incisions and drainage were reported. Patients who have severe dermatologic reactions or who

develop worsening reactions whilst receiving Vectibix should be monitored for the development of inflammatory or infectious sequelae, and appropriate treatment promptly initiated.

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. [see **Dosage and Administration (2.3), Warnings and Precautions (5.1), and Adverse Reactions (6.1)**].

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 six 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 two 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 ($\geq 20\%$) 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 ($\geq 20\%$) in patients with wild-type *KRAS* mCRC receiving Vectibix (6 mg/kg every two 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 ($\geq 2\%$ 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.

About XGEVA® (denosumab)

XGEVA in the European Union

In the European Union, XGEVA is approved for the prevention of skeletal-related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with bone metastases from solid tumours. XGEVA is also approved for the treatment of adults and skeletally mature adolescents with giant cell tumour of bone that is unresectable or where surgical resection is likely to result in severe morbidity.

Special Warnings and Precautions: Pre-existing hypocalcaemia must be corrected prior to initiating therapy with XGEVA. Hypocalcaemia can occur at any time during therapy. Monitor calcium prior to initial dose, within two weeks of initial dose and if suspected symptoms of hypocalcaemia occur. Severe symptomatic hypocalcaemia has been reported. Consider additional monitoring of calcium level in patients with risk factors for hypocalcaemia or if otherwise indicated based on clinical condition of the patient. Patients with severe renal impairment (creatinine clearance $< 30\text{ml/min}$) or receiving dialysis are at greater risk of developing hypocalcaemia; this risk and accompanying elevations in parathyroid hormone increases with increasing degree of renal impairment. Regular monitoring of calcium levels in these patients is especially important. If hypocalcaemia occurs while receiving XGEVA, additional calcium supplementation and additional monitoring may be necessary. Osteonecrosis of the jaw (ONJ) has occurred commonly in patients treated with XGEVA. Delay treatment in patients with unhealed open soft tissue lesions in the mouth. A dental examination with preventive dentistry and an individual benefit-risk assessment is recommended prior to treatment. Refer to the SmPC for risk factors for ONJ. Patients should be encouraged to maintain good oral hygiene, receive routine dental check-ups and immediately report oral symptoms during treatment with XGEVA. While on treatment, invasive dental procedures should be performed only after careful consideration and avoided in close proximity to XGEVA administration. The management plan of patients who develop ONJ should be set up in close collaboration between the treating physician and a dentist or oral surgeon with expertise in ONJ. Atypical femoral fracture (AFF) has been reported in patients receiving XGEVA. Discontinuation of XGEVA therapy in patients suspected to have AFF should be considered pending evaluation of the patient based on an individual benefit risk assessment. Patients being treated with XGEVA should not be treated concomitantly with other denosumab containing medicinal products (for osteoporosis indications) or with bisphosphonates. Patients with rare hereditary problems of fructose intolerance should not use XGEVA.

Adverse reactions in patients receiving XGEVA to prevent the occurrence of skeletal related events: very common ($\geq 1/10$) dyspnoea, diarrhoea and musculoskeletal pain; common ($\geq 1/100$ to $< 1/10$) hypocalcaemia, hypophosphataemia, tooth extraction, hyperhidrosis and osteonecrosis of the jaw; rare ($\geq 1/10,000$ to $< 1/1000$) drug hypersensitivity, anaphylactic reaction, atypical femoral fracture. In three phase III clinical trials, ONJ was confirmed in 1.8% of patients treated with XGEVA and 1.3% of patients treated with zoledronic acid (primary treatment phase). Among subjects with confirmed ONJ, most (81% in both treatment groups) had a history of tooth extraction, poor oral hygiene, and/or use of a dental appliance. Hypocalcaemia was reported in 9.6% of patients treated with XGEVA and 5.0% of patients treated with zoledronic acid. Neutralizing antibodies have not been observed in clinical studies. In the postmarketing setting, severe symptomatic hypocalcaemia (including fatal cases), hypersensitivity (including rare events of anaphylactic reaction) and musculoskeletal pain (including severe cases) have been reported. Please consult the SmPC for a full description of undesirable effects.

Contraindications: Severe, untreated hypocalcaemia; hypersensitivity to the active substance or to any of the excipients; unhealed lesions from dental or oral surgery.

XGEVA in the U.S.

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, which were defined as radiation to bone, pathologic fracture, surgery to the bone, and spinal cord compression. XGEVA is administered as a single subcutaneous injection of 120 mg once every four 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. XGEVA is administered as a single subcutaneous injection of 120 mg once every four weeks with additional 120 mg doses administered on days eight and 15 of the first month of therapy.

In 2014, XGEVA was approved by the FDA for the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy. XGEVA is administered as a single subcutaneous injection of 120 mg once every four weeks with additional 120 mg doses administered on days eight and 15 of the first month of 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, especially in the first weeks of initiating therapy, and administer calcium, magnesium, and vitamin D as necessary. Monitor levels more frequently when XGEVA is administered with other drugs that can also lower calcium levels. Advise patients to contact a healthcare professional for symptoms of hypocalcemia.

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

Hypersensitivity

XGEVA is contraindicated in patients with known clinically significant hypersensitivity to XGEVA, including anaphylaxis that has been reported with use of XGEVA. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue XGEVA therapy permanently.

Drug Products with Same Active Ingredient

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

Osteonecrosis of the Jaw

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

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

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

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

Atypical Subtrochanteric and Diaphyseal Femoral Fracture

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

Atypical femoral fractures most commonly occur with minimal or no trauma to the affected area. They may be bilateral and many patients report prodromal pain in the affected area, usually presenting as dull, aching thigh pain, weeks to months before a complete fracture occurs. A number of reports note that patients were also receiving treatment with glucocorticoids (e.g. prednisone) at the time of fracture. During XGEVA treatment, patients should be advised to report new or unusual thigh, hip, or groin pain. 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. XGEVA can cause fetal harm when administered to a pregnant woman. Based on findings in animals, XGEVA is expected to result in adverse reproductive effects. Advise females of reproductive potential to use highly effective contraception during therapy, and for at least five months after the last dose of XGEVA. Apprise the patient of the potential hazard to a fetus if XGEVA is used during pregnancy or if the patient becomes pregnant while patients are exposed to XGEVA.

Adverse Reactions

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

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

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

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

About Neulasta® (pegfilgrastim)

Neulasta is a leukocyte growth factor approved by the FDA and in the EU 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.

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 ($\geq 5\%$ 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 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) 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 Amgen's business. Unless otherwise noted, Amgen is providing this information as of Sept. 14, 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 Amgen projects. 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 Amgen and its partners to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and Amgen expects similar variability in the future. Amgen develops 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 Amgen may have believed at the time of entering into such relationship. Also, Amgen or others could identify safety, side effects or manufacturing problems with Amgen's products after they are on the market. Amgen's business may be impacted by government investigations, litigation and product liability claims. If Amgen fails to meet the compliance obligations in the corporate integrity agreement between Amgen and the U.S. government, Amgen could become subject to significant sanctions. Amgen depends on third parties for a significant portion of its manufacturing capacity for the supply of certain of its current and future products and limits on supply may constrain sales of certain of its current products and product candidate development.

In addition, sales of Amgen's products (including products of Amgen's 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 Amgen's products. In addition, Amgen competes with other companies with respect to some of its marketed products as well as for the discovery and development of new products. Amgen believes that some of its newer products, product candidates or new indications for existing products, may face competition when and as they are approved and marketed. Amgen's products may compete against products that have lower prices, established reimbursement, superior performance, are easier to administer, or that are otherwise competitive with its products. In addition, while Amgen and its partners routinely obtain patents for their products and technology, the protection of Amgen's products offered by patents and patent applications may be challenged, invalidated or circumvented by its competitors and there can be no guarantee of Amgen's or its partners' ability to obtain or maintain patent protection for Amgen's products or product candidates. Amgen cannot guarantee that it will be able to produce commercially successful products or maintain the commercial success of its existing products. Amgen's stock price may be affected by actual or perceived market opportunity, competitive position and success or failure of its products or product candidates. Further, the discovery of significant problems with a product similar to one of Amgen's products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on Amgen's business and results of operations. Amgen's efforts to integrate the operations of companies it has acquired may not be successful. Amgen may experience difficulties, delays or unexpected costs and not achieve anticipated cost savings from its ongoing restructuring plan. Amgen's business performance could affect or limit the ability of Amgen's Board of Directors to declare a dividend or their ability to pay a dividend or repurchase Amgen 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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