



Amgen Highlights Data To Be Presented At ASCO 2017 Across Oncology Portfolio

May 17, 2017

Oral Presentation of New Analysis on Limited Renal Toxicity Associated With XGEVA® (denosumab) Compared With Zoledronic Acid in Treatment of Myeloma Bone Disease **XGEVA Study in Patients With Myeloma Bone Disease Also Selected for Best of ASCO®** **First Randomized Study to Evaluate the Combination of IMLYGIC® (talimogene laherparepvec), an Oncolytic Viral Immunotherapy, With a Checkpoint Inhibitor to be Presented**

THOUSAND OAKS, Calif., May 17, 2017 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that new clinical data and analyses from across its oncology portfolio will be presented at the 53rd Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago, June 2-6, 2017.

"At Amgen, we are committed to translating science into innovative and effective treatments for cancer patients across the disease continuum," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "The data that will be presented at this year's ASCO meeting highlight the potential of our marketed products in new patient populations and in combination with other therapies."

Amgen data to be presented at ASCO include an oral presentation of results from the Phase 3 '482 study, evaluating the efficacy and safety of XGEVA® (denosumab) in a head-to-head comparison with zoledronic acid for the prevention of fractures and other bone complications in patients with newly diagnosed multiple myeloma. This abstract was also selected for inclusion in the Best of ASCO® educational program, designed to increase global access to cutting-edge science. Current treatment options for bone complications are limited to bisphosphonates, which are associated with renal toxicity.

Impact of Denosumab (DMB) Compared With Zoledronic Acid (ZA) on Renal Function in the Treatment of Myeloma Bone Disease

Abstract #8005, Oral Presentation, Sunday, June 4 at 9:45 a.m. CT in McCormick Place, 354b

New IMLYGIC® (talimogene laherparepvec) data will be presented, including the primary analysis of a Phase 2 study evaluating IMLYGIC in combination with an immune checkpoint inhibitor:

- **Primary Results From a Randomized (1:1), Open-Label Phase 2 Study of Talimogene Laherparepvec (T) and Ipilimumab (I) Versus I Alone in Unresected Stage IIIB- IV Melanoma**
Abstract #9509, Poster Discussion, Saturday, June 3 at 4:45 p.m. CT in McCormick Place, 354b
- **Humanistic Burden of Disease in Earlier Stage Metastatic (Stage IIIB/C-IVM1A) Versus Late Stage Metastatic (IVM1B/C) Melanoma Patients in a Real World Setting in the US**
Abstract #9561, Poster Presentation, Saturday, June 3 at 1:15 p.m. CT in McCormick Place, Hall A

Two abstracts will be presented on BLINCYTO® (blinatumomab), the first-and-only approved CD19-directed CD3 bispecific T cell engager (BiTE®) immunotherapy:

- **Blinatumomab Use in Pediatric Patients (Pts) With Relapsed/Refractory B-precursor Acute Lymphoblastic Leukemia (R/R ALL) From an Open-label, Multicenter, Expanded Access Study**
Abstract #10530, Poster Presentation, Sunday, June 4 at 8 a.m. CT in McCormick Place, Hall A
- **Exposure-adjusted Adverse Events (AEs) Comparing Blinatumomab to Standard of Care (SOC) Chemotherapy in Patients (Pts) With Relapsed/Refractory B-precursor Acute Lymphoblastic Leukemia (R/R ALL) From a Randomized Phase III Study**
Abstract #7032, Poster Presentation, Monday, June 5 at 8 a.m. CT in McCormick Place, Hall A

KYPROLIS® (carfilzomib) is the first and only multiple myeloma therapy to demonstrate superior overall survival, reducing the risk of death by 21 percent, in a head-to-head comparison with Velcade® (bortezomib) when each was added to dexamethasone in the relapsed setting.¹ The KYPROLIS clinical development program is focused on providing solutions for physicians and patients in treating multiple myeloma. Data at ASCO include:

- **Rates of Peripheral Neuropathy (PN) in Patients (Pts) With Relapsed and Refractory Multiple Myeloma (RRMM) Treated With Carfilzomib vs Comparators in Pivotal Phase 3 Trials**
Abstract #8041, Poster Presentation, Monday, June 5 at 8 a.m. CT in McCormick Place, Hall A

Presentations featuring Vectibix® (panitumumab) data will include:

- **Profiling Circulating Tumor DNA (ctDNA) Mutations After Panitumumab Treatment in Patients With Refractory Metastatic Colorectal Cancer (mCRC) From the Phase III ASPECCT Study**
Abstract #3523, Poster Discussion, Saturday, June 3 at 1:15 p.m. CT in McCormick Place, Arie Crown Theater
- **Early Tumor Shrinkage (ETS) and Depth of Response (DpR) in Wild-Type (WT) RAS Tumors from the Phase III Trial of Panitumumab (Pmab) Plus Best Supportive Care (BSC) Versus BSC in Chemorefractory Metastatic Colorectal Cancer (mCRC)**

Abstract #3561, Poster Presentation, Saturday, June 3 at 8 a.m. CT in McCormick Place, Hall A

- **Clinical Outcomes and Emergent Circulating Tumor (Ct) DNA RAS Mutations and Allele Fraction for Patients With Metastatic Colorectal Cancer (mCRC) Treated With Panitumumab from the ASPECCT Study**

Abstract #3584, Poster Presentation, Saturday, June 3 at 8 a.m. CT in McCormick Place, Hall A

Data will be presented on the investigational agent ABP 215, which is being developed as a bevacizumab biosimilar:

- **Clinical Comparison of ABP 215 and Bevacizumab in Patients With NSCLC: Pharmacokinetic Results and Justification for Extrapolation Across Bevacizumab Indications**

Abstract #9050, Poster Presentation, Saturday, June 3 at 8 a.m. CT in McCormick Place, Hall A

Abstracts are currently available on the ASCO website.

About XGEVA® (denosumab)

XGEVA 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 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. XGEVA is also indicated in the U.S. for the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy. XGEVA is not indicated for the prevention of SREs in patients with multiple myeloma.

U.S. Important Safety Information

Hypocalcemia

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

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

Hypersensitivity

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

Drug Products with Same Active Ingredient

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

Osteonecrosis of the Jaw

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

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

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

Atypical Subtrochanteric and Diaphyseal Femoral Fracture

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

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

Hypercalcemia Following Treatment Discontinuation in Patients with Growing Skeletons

Clinically significant hypercalcemia has been reported in XGEVA® treated patients with growing skeletons, weeks to months following treatment discontinuation. Monitor patients for signs and symptoms of hypercalcemia and treat appropriately.

Embryo-Fetal Toxicity

XGEVA[®] can cause fetal harm when administered to a pregnant woman. Based on findings in animals, XGEVA[®] is expected to result in adverse reproductive effects. Advise females of reproductive potential to use highly effective contraception during therapy, and for at least 5 months after the last dose of XGEVA[®]. Apprise the patient of the potential hazard to a fetus if XGEVA[®] is used during pregnancy or if the patient becomes pregnant while patients are exposed to XGEVA[®].

Adverse Reactions

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

The most common adverse reactions resulting in discontinuation were osteonecrosis and hypocalcemia. 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 U.S. Prescribing Information.

About IMLYGIC[®]

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 U.S. 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 in patients who have underlying autoimmune disease or before continuing treatment in patients who develop immune-mediated events.
- **Plasmacytoma at the Injection Site:** Plasmacytoma in proximity to the injection site has been reported in a patient with smoldering multiple myeloma after IMLYGIC[®] administration in a clinical study. Consider the risks and benefits of IMLYGIC[®] in patients with multiple myeloma or in whom plasmacytoma develops during treatment.
- **Obstructive Airway Disorder:** Obstructive airway disorder has been reported following IMLYGIC[®] treatment. Use caution when injecting lesions close to major airways.

Adverse Reactions

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

Please see full [Prescribing Information](#) and [Medication Guide](#) for IMLYGIC[®].

About BLINCYTO[®] (blinatumomab)

BLINCYTO is a bispecific CD19-directed CD3 T cell engager (BiTE[®]) antibody construct that binds specifically to CD19 expressed on the surface of cells of B-lineage origin and CD3 expressed on the surface of T cells.

BLINCYTO was granted breakthrough therapy and priority review designations by the FDA, and is now approved in the U.S. for the treatment of Philadelphia chromosome-negative (Ph-) relapsed or refractory B-cell precursor ALL. This indication is approved under accelerated approval. Continued approval for this indication may be contingent upon verification of clinical benefit in subsequent trials.

In November 2015, BLINCYTO was granted conditional marketing authorization in the EU for the treatment of adults with Ph- relapsed or refractory B-cell precursor ALL.

About BiTE[®] Technology

Bispecific T cell engager (BiTE[®]) antibody constructs are a type of immunotherapy being investigated for fighting cancer by helping the body's immune system to detect and target malignant cells. The modified antibodies are designed to engage two different targets simultaneously, thereby juxtaposing T cells (a type of white blood cell capable of killing other cells perceived as threats) to cancer cells. BiTE[®] antibody constructs help place the T cells within reach of the targeted cell, with the intent of allowing T cells to inject toxins and trigger the cancer cell to die (apoptosis). BiTE[®] antibody constructs are currently being investigated for their potential to treat a wide variety of cancers. For more information, visit www.biteantibodies.com.

BLINCYTO[®] U.S. Product Safety Information

Important Safety Information Regarding BLINCYTO[®] (blinatumomab) U.S. Indication

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):** CRS, which may be life-threatening or fatal, 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 64% of patients receiving BLINCYTO[®] in clinical trials experienced neurological toxicities. The median time to onset of any neurological toxicity was 4 days. The most common (≥ 10%) manifestations of

neurological toxicity were headache, tremor, dizziness, and altered state of consciousness. Severe, life-threatening, or fatal neurological toxicities occurred in approximately 17% of patients, including encephalopathy, convulsions, speech disorders, disturbances in consciousness, confusion and disorientation, and coordination and balance disorders. The neurological toxicity profile varied by age group. 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): TLS, which may be life-threatening or fatal, 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 have been associated with BLINCYTO® treatment with a median time to onset of 3 days. In patients receiving BLINCYTO®, although the majority of these events were observed in the setting of CRS, some cases of elevated liver enzymes were observed outside the setting of CRS, with a median time to onset of 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 TBIL 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 TBIL rises to > 3 times ULN.
- Pancreatitis: Fatal pancreatitis has been reported in patients receiving BLINCYTO® in combination with dexamethasone in clinical trials and the post-marketing setting. Evaluate patients who develop signs and symptoms of pancreatitis and interrupt or discontinue BLINCYTO® and dexamethasone as needed.
- 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 antileukemic chemotherapy.
- Preparation and administration errors have occurred with BLINCYTO® treatment. Follow instructions for preparation (including admixing) and administration in the PI strictly to minimize medication errors (including underdose and overdose).
- Immunization: Vaccination with live virus vaccines is not recommended for at least 2 weeks prior to the start of BLINCYTO® treatment, during treatment, and until immune recovery following last cycle of BLINCYTO®.

Adverse Reactions

- The most common adverse reactions ($\geq 20\%$) in the safety population studied in clinical trials were pyrexia (66%), headache (34%), nausea (27%), edema (26%), hypokalemia (26%), anemia (25%), febrile neutropenia (24%), neutropenia (22%), thrombocytopenia (20%), and abdominal pain (20%). The safety population included 225 patients weighing 45 kg or more and 57 patients weighing less than 45 kg. For some adverse reactions, there were differences in the incidence rates by age subgroup.
- In patients weighing greater than or equal to 45 kg, serious adverse reactions were reported in 61% of patients. The most common serious adverse reactions ($\geq 2\%$) included febrile neutropenia (9%), pyrexia (6%), sepsis (5%), pneumonia (5%), device-related infection (4%), neutropenia (3%), tremor (3%), overdose (3%), encephalopathy (3%), infection (2%), confusion (3%) and headache (2%).
- In patients weighing less than 45 kg, serious adverse reactions were reported in 51% of patients. The most common serious adverse reactions ($\geq 2\%$) included pyrexia (12%), febrile neutropenia (9%), cytokine release syndrome (4%), convulsion (4%), device-related infection (4%), hypoxia (4%), sepsis (4%), and overdose (4%).

U.S. 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, including **Boxed WARNINGS** and Medication Guide, for BLINCYTO® at www.BLINCYTO.com.

About KYPROLIS® (carfilzomib)

Proteasomes play an important role in cell function and growth by breaking down proteins that are damaged or no longer needed.² 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.^{2,3}

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, Australia, Bahrain, Canada, Hong Kong, Israel, Japan, Kuwait, Lebanon, Macao, Mexico, Thailand, Colombia, S. Korea, Canada, Qatar, Switzerland, United Arab Emirates, Turkey, Russia, Brazil, India, Oman and the European Union. Additional regulatory applications for KYPROLIS are underway and have been submitted to health authorities worldwide.

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.
- Patients \geq 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.

Hemorrhage

- Fatal or serious cases of hemorrhage have been reported in patients receiving KYPROLIS. Hemorrhagic events have included gastrointestinal, pulmonary, and intracranial hemorrhage and epistaxis. Promptly evaluate signs and symptoms of blood loss. Reduce or withhold dose as appropriate.

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 neuro-radiological 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 reactions 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 reactions 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 Vectibix® (panitumumab)

Vectibix is the first fully human monoclonal anti-EGFR antibody approved by the FDA for the treatment of mCRC. Vectibix was approved in the U.S. in September 2006 as a monotherapy for the treatment of patients with EGFR-expressing mCRC after disease progression after prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy.

In May 2014, the FDA approved Vectibix for use in combination with FOLFOX, as first-line treatment in patients with wild-type *KRAS* (exon 2) mCRC. With this approval, Vectibix became the first-and-only biologic therapy indicated for use with FOLFOX, one of the most commonly used chemotherapy regimens, in the first-line treatment of mCRC for patients with wild-type *KRAS* mCRC.

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% 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 Vectibix®. Life-threatening and fatal bullous mucocutaneous disease with blisters, erosions and skin sloughing has also been observed in patients treated with Vectibix®. It could not be determined whether these mucocutaneous adverse reactions were directly related to EGFR inhibition or to idiosyncratic immune-related effects (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 ($\geq 20\%$) 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 ($> 20\%$) 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.

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 for which 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.

About Amgen

Amgen is committed to unlocking the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing and delivering innovative human therapeutics. This approach begins by using tools like advanced human genetics to unravel the complexities of disease and understand the fundamentals of human biology.

Amgen focuses on areas of high unmet medical need and leverages its expertise to strive for solutions that improve health outcomes and dramatically improve people's lives. A biotechnology pioneer since 1980, Amgen has grown to be one of the world's leading independent biotechnology companies, has reached millions of patients around the world and is developing a pipeline of medicines with breakaway potential.

For more information, visit www.amgen.com and follow us on www.twitter.com/amgen.

Forward-Looking Statements

This news release contains forward-looking statements that are based on the current expectations and beliefs of Amgen. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission reports filed by Amgen, including our most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and 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. Certain of our distributors, customers and payers have substantial purchasing leverage in their dealings with us. The discovery of significant problems with a product similar to one of our products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on our business and results of operations. Our efforts to acquire other companies or products and to integrate the operations of companies we have acquired may not be successful. 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 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 not part of the labeling approved by the FDA for the products.

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