Amgen Receives CHMP Positive Opinions For Two New Treatment Options For Patients With Blood Cancer In Europe

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Pivotal Study Demonstrated Kyprolis® (Carfilzomib) in Combination With Standard of Care can Extend Time Patients Live Without Disease Progressing

BLINCYTO® (Blinatumomab) is First Bispecific T cell Engager (BiTE®) Antibody Construct to be Granted Positive CHMP Opinion

THOUSAND OAKS, Calif., Sept. 25, 2015 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted positive opinions recommending marketing authorization for:

- Kyprolis® (carfilzomib) in combination with lenalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.
- BLINCYTO® (blinatumomab) as a conditional marketing authorization for the treatment of adults with Philadelphia chromosome-negative (Ph-) relapsed or refractory B-precursor acute lymphoblastic leukemia (ALL).

"We are pleased to receive positive CHMP opinions for Kyprolis and BLINCYTO as this is an important step in providing new treatment options for patients in Europe with rare forms of cancer," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "For patients with multiple myeloma, periods of remission become shorter following each new treatment regimen, underscoring the need for additional treatment options. The results of the ASPIRE study demonstrate that Kyprolis extended the time patients live without their disease progressing. Additionally, there is a critical need for new therapies for patients with relapsed or refractory B-cell precursor ALL."

Kyprolis is a proteasome inhibitor for use in the treatment of patients with relapsed multiple myeloma. Proteasomes play an important role in cell function and growth by breaking down proteins that are damaged or no longer needed. Kyprolis blocks proteasomes, which leads to an excessive build-up of proteins within cells. 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.

BLINCYTO is the first clinical validation of the bispecific T cell engager (BiTE®) platform, an innovative approach that can help the body's own immune system fight cancer.

The CHMP positive opinions will now be reviewed by the European Commission and if granted, the two products will have marketing authorization in the 28 member countries of the European Union (EU), as well as Iceland, Lichtenstein and Norway.

About Multiple Myeloma

Multiple myeloma is an incurable blood cancer, characterized by a recurring pattern of remission and relapse. Multiple myeloma is an orphan disease and accounts for approximately 1 percent of all cancers[1,2].

About Kyprolis® (carfilzomib)

Kyprolis was granted orphan drug designation by the EMA in 2008, and in February 2015, its Marketing Authorization Application (MAA) was granted accelerated assessment by the EMA. Kyprolis® (carfilzomib) for Injection was approved as a monotherapy in the U.S. in July 2012, and in combination with lenalidomide and dexamethasone in July 2015. Kyprolis is also approved in Argentina, Israel, Kuwait, Mexico and Thailand.

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

For more information about Kyprolis, visit www.kyprolis.com.

About Kyprolis European Marketing Authorization Application

The MAA was based on data from the Phase 3 ASPIRE (C**A**rfilzomib, Lenalidomide, and Dexametha**S**one versus Lenalidomide and Dexamethasone for the treatment of **P**at**I**ents with **R**elapsed Multiple My**E**loma) trial. The study showed that patients treated with Kyprolis in combination with lenalidomide and dexamethasone (regimen referred to as KRd) had increased median time to progressive disease (PD) or death by 8.7 months compared to patients treated with lenalidomide and dexamethasone (regimen referred to as Rd) (26.3 months for KRd compared to 17.6 months for Rd with HR=0.69; 95 percent CI: 0.57-0.83; 1-sided $p<0.0001$). Discontinuation of treatment due to adverse events (AEs) occurred in 15 percent of patients in the KRd arm versus 18 percent of patients in the Rd arm.

About ASPIRE

The international, randomized Phase 3 ASPIRE trial evaluated Kyprolis in combination with lenalidomide and dexamethasone, versus lenalidomide and dexamethasone alone, in patients with relapsed multiple myeloma following treatment with one to three prior regimens. The primary endpoint of the trial was progression-free survival (PFS), defined as the time from randomization to disease progression or death due to any cause, whichever is earlier. The study showed that patients treated with Kyprolis in combination with lenalidomide and low-dose dexamethasone had increased median time to PD or death by 8.7 months compared to patients treated with lenalidomide and dexamethasone (26.3 months for KRd compared to 17.6 months for Rd with HR=0.69; 95 percent CI: 0.57-0.83; 1-sided $p<0.0001$). Secondary endpoints included overall survival (OS), overall response rate (ORR), duration of response (DOR), disease control rate, health-related quality of life (HR-QoL) and safety. Patients were randomized to receive Kyprolis (20 mg/m^2 on days 1 and 2 of cycle one only, escalating to 27 mg/m^2 subsequently), in addition to a standard dosing schedule of lenalidomide (25 mg per day for 21 days on, 7 days off) and dexamethasone (40 mg per week in 4 week cycles), versus lenalidomide and dexamethasone alone. In the Kyprolis arm, patients were given a 10 minute infusion on days 1, 2, 8, 9, 15 and 16. Kyprolis was omitted on days 8 and 9 during cycles 13-18 and

not administered beyond 18 cycles. The study randomized 792 patients at sites in North America, Europe and Israel.

While the data for median OS are not yet mature based on the prespecified statistical boundary at the interim (1-sided p-value of smaller than 0.0051), the analysis showed a trend in favor of KRd compared with Rd (HR=0.79; 95 percent CI: 0.63-0.99; one-sided *p*=0.018, two-sided *p*=0.04). Patients continue to be monitored for OS. The ORR was 87.1 percent with KRd and 66.7 percent with Rd. Median DOR was 28.6 months for patients receiving KRd (95 percent CI, 24.9 to 31.3 months) and 21.2 months for patients receiving Rd (95 percent CI, 16.7 to 25.8 months). In the KRd and Rd groups, 32 percent versus 9 percent of patients achieved a complete response or higher (stringent complete response [sCR] or complete response [CR]), a measurement indicating depth of response.

The rate of deaths due to AEs within 30 days of the last dose was balanced between the KRd arm and the Rd arm. The most common causes of death not due to PD occurring in patients in the KRd arm compared to the Rd arm included cardiac disorders (3 percent versus 2 percent), infection (2 percent versus 3 percent), renal (0 percent versus less than 1 percent) and other AEs (2 percent versus 3 percent). Serious AEs were reported in 60 percent of the patients in the KRd arm and 54 percent of the patients in the Rd arm. The most common serious AEs reported in the KRd arm compared to the Rd arm were pneumonia (14 percent versus 11 percent), respiratory tract infection (4 percent versus 2 percent), pyrexia (4 percent versus 2 percent) and pulmonary embolism (3 percent versus 2 percent). Discontinuation of treatment due to AEs occurred in 15 percent of patients in the KRd arm versus 18 percent of patients in the Rd arm. AEs leading to discontinuation of Kyprolis occurred in 12 percent of patients and the most common events included pneumonia (1 percent), myocardial infarction (1 percent) and upper respiratory tract infection (1 percent).

The ASPIRE data were presented at the 56th Annual Meeting of the American Society of Hematology and published in *The New England Journal of Medicine* in December 2014.[3]

About Acute Lymphoblastic Leukemia (ALL)
It is estimated that there are close to 600 adults with Ph- relapsed or refractory B-precursor ALL in France, Germany, Italy, Spain, and the U.K.[4]

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.

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.

BLINCYTO was granted breakthrough therapy and priority review designations by the U.S. Food and Drug Administration, and is now approved in the U.S. for the treatment of 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.

About BLINCYTO European Conditional Marketing Authorization Application
The CHMP recommended granting BLINCYTO a conditional marketing authorization for the treatment of adults with Ph- relapsed or refractory B-precursor ALL.

Conditional license requires the license to be renewed every year and it will be converted to full standard license once post-licensing commitments have been fulfilled. Amgen expects a decision on the conditional MAA from the European Commission in the coming months.

The BLINCYTO conditional marketing authorization application is based on results of the '211 and '206 trials. In the '211 study:

- 42.9 percent of evaluable patients receiving BLINCYTO achieved complete remission or complete remission with partial hematological recovery (CR/CRh*).
- 17 percent of patients underwent allogeneic hematopoietic stem cell transplantation (HSCT) in CR/CRh* induced with BLINCYTO
- 82.2 percent of those who achieved CR/CRh* achieved deep molecular remission, or minimal residual disease (MRD) response, a measure of eradication of residual disease at the molecular level.
- The most serious adverse reactions included: infections (31.7 percent), neurologic events (16.4 percent), neutropenia/febrile neutropenia (15.3 percent), cytokine release syndrome (0.5 percent) and tumor lysis syndrome (0.5 percent).

About Study '211
Study '211 evaluated blinatumomab in an open-label, multicenter, single-arm Phase 2 study. Eligible patients were at least 18 years of age with Ph- relapsed or refractory B-precursor ALL. Relapsed or refractory was defined as relapsed with a first remission duration of less than or equal to 12 months in first salvage, or relapsed or refractory after the first salvage, or relapsed within 12 months of allogeneic hematopoietic stem cell transplantation (HSCT), and greater than or equal to 10 percent blasts in bone marrow. The primary endpoint was the CR/CRh* rate within two cycles of blinatumomab. Of the 189 patients evaluated in the trial, 42.9 percent (81/189; 95 percent CI, 35.7 – 50.2) achieved CR or CRh* within two cycles of treatment with blinatumomab with the majority of responses (79 percent [64/81]) occurring within the first cycle of treatment. In a prespecified exploratory analysis, 82.2 percent (60/73) of MRD evaluable patients with CR/CRh* also had a MRD response. The most common adverse reactions (greater than 20 percent) were infusion-related reactions (67.2 percent), infections (63 percent), pyrexia (59.8 percent), headache (34.4 percent), febrile neutropenia (28 percent), peripheral edema (25.9 percent), nausea (24.3 percent), hypokalemia (23.8 percent), constipation (20.6 percent) and anemia (20.1 percent). The most serious adverse reactions that occurred during blinatumomab treatment included: infections (31.7 percent), neurologic events (16.4 percent), neutropenia/febrile neutropenia (15.3 percent), cytokine release syndrome (0.5 percent) and tumor lysis syndrome (0.5 percent).

About Study '206
Study '206 evaluated the safety and efficacy of blinatumomab in an open-label, multicenter, dose-escalation Phase 2 study of 36 patients, who were at least 18 years of age with B-precursor ALL relapsed after at least induction and consolidation or having refractory disease with greater than 5 percent blasts in bone marrow, had an Eastern Cooperative Oncology Group (ECOG) performance status of at most 2, had a life expectancy of at least 12 weeks, and who did not have autologous HSCT within six weeks prior to start of treatment, allogeneic HSCT within three months prior to start of treatment, or previous treatment with blinatumomab.

The CR/CRh* rate was 69.4 percent (25/36) with 15 patients achieving CR (41.7 percent; 95 percent CI, 25.5 percent - 59.2 percent), and 10 patients achieving CRh* (27.8 percent; 95 percent CI, 14.2 percent - 45.2 percent). Of the patients with hematologic CR, 88 percent (22/25) also had MRD responses. The median duration of remission was 8.9 months, and the median relapse-free survival (RFS) was 7.6 months. The median OS was 9.8 months. Overall safety results from this study were consistent with the known blinatumomab safety profile.

Kyprolis U.S. Product Safety Information

Important Safety Information Regarding Kyprolis (carfilzomib) for Injection U.S. Indication
This safety information is specific to the current U.S. approved indication

Cardiac Toxicities
New onset or worsening of pre-existing cardiac failure (e.g., congestive heart failure, pulmonary edema, and decreased ejection fraction), restrictive cardiomyopathy, myocardial ischemia, and myocardial infarction including fatalities have occurred following administration of Kyprolis. Death due to cardiac arrest has occurred within a day of Kyprolis administration.

Withhold Kyprolis for Grade 3 or 4 cardiac adverse events until recovery, and consider whether to restart Kyprolis based on a benefit/risk assessment.

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 ≥ 75 years, the risk of cardiac failure is increased. Patients with New York Heart Association Class III and IV heart failure, recent myocardial infarction, and conduction abnormalities may be at greater risk for cardiac complications.

Acute Renal Failure
Cases of acute renal failure and renal insufficiency adverse events (renal impairment, acute renal failure, and 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. This risk was greater in patients with a baseline reduced estimated creatinine clearance. 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 and should be based on an assessment of the patient's underlying risks, treatment regimen, and clinical status.

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

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

Hepatic Toxicity and Hepatic Failure
Cases of hepatic failure, including fatal cases, have been reported during treatment with Kyprolis. Kyprolis can cause increased serum transaminases.

Monitor liver enzymes regularly. Reduce or withhold dose as appropriate.

Thrombotic Thrombocytopenic Purpura /Hemolytic Uremic Syndrome (TTP/HUS)
Cases of 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 and the potential hazard to the fetus if Kyprolis is used during pregnancy.

ADVERSE REACTIONS
The most common adverse events occurring in at least 20% of patients treated with Kyprolis in monotherapy trials: anemia, fatigue, thrombocytopenia, nausea, pyrexia, decreased platelets, dyspnea, diarrhea, decreased lymphocyte, headache, decreased hemoglobin, cough, edema peripheral.

The most common adverse events occurring in at least 20% of patients treated with Kyprolis in the combination therapy trial: decreased lymphocytes, decreased absolute neutrophil count, decreased phosphorus, anemia, neutropenia, decreased total white blood cell count, decreased platelets, diarrhea, fatigue, thrombocytopenia, pyrexia, muscle spasm, cough, upper respiratory tract infection, decreased hemoglobin, hypokalemia.

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

BLINCYTO U.S. Product Safety Information
Important Safety Information Regarding BLINCYTO® (blinatumomab) U.S. Indication
This safety information is specific to the current U.S. approved 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): Life-threatening or fatal CRS occurred in patients receiving BLINCYTO®. Infusion reactions have occurred and may be clinically indistinguishable from manifestations of CRS. Closely monitor patients for signs and symptoms of serious events such as pyrexia, headache, nausea, asthenia, hypotension, increased alanine aminotransferase (ALT), increased aspartate aminotransferase (AST), increased total bilirubin (TBILI), disseminated intravascular coagulation (DIC), capillary leak syndrome (CLS), and hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS). Interrupt or discontinue BLINCYTO® as outlined in the Prescribing Information (PI).

Neurological Toxicities: Approximately 50% of patients receiving BLINCYTO® in clinical trials experienced neurological toxicities. Severe, life-threatening, or fatal neurological toxicities occurred in approximately 15% of patients, including encephalopathy, convulsions, speech disorders, disturbances in consciousness, confusion and disorientation, and coordination and balance disorders. The median time to onset of any neurological toxicity was 7 days. Monitor patients for signs or symptoms and interrupt or discontinue BLINCYTO® as outlined in the PI.

Infections: Approximately 25% of patients receiving BLINCYTO® experienced serious infections, some of which were life-threatening or fatal. Administer prophylactic antibiotics and employ surveillance testing as appropriate during treatment. Monitor patients for signs or symptoms of infection and treat appropriately, including interruption or discontinuation of BLINCYTO® as needed.

Tumor Lysis Syndrome (TLS): Life-threatening or fatal TLS has been observed. Preventive measures, including pretreatment nontoxic cytoreduction and on treatment hydration, should be used during BLINCYTO® treatment. Monitor patients for signs and symptoms of TLS and interrupt or discontinue BLINCYTO® as needed to manage these events.

Neutropenia and Febrile Neutropenia, including life-threatening cases, have been observed. Monitor appropriate laboratory parameters during BLINCYTO® infusion and interrupt BLINCYTO® if prolonged neutropenia occurs.

Effects on Ability to Drive and Use Machines: Due to the possibility of neurological events, including seizures, patients receiving BLINCYTO® are at risk for loss of consciousness, and should be advised against driving and engaging in hazardous occupations or activities such as operating heavy or potentially dangerous machinery while BLINCYTO® is being administered.

Elevated Liver Enzymes: Transient elevations in liver enzymes have been associated with BLINCYTO® treatment. The majority of these events were observed in the setting of CRS. The median time to onset was 15 days. Grade 3 or greater elevations in liver enzymes occurred in 6% of patients outside the setting of CRS and resulted in treatment discontinuation in less than 1% of patients. Monitor ALT, AST, gamma-glutamyl transferase (GGT), and TBILI prior to the start of and during BLINCYTO® treatment. BLINCYTO® treatment should be interrupted if transaminases rise to > 5

times the upper limit of normal (ULN) or if TBILI rises to > 3 times ULN.

Leukoencephalopathy: Although the clinical significance is unknown, cranial magnetic resonance imaging (MRI) changes showing leukoencephalopathy have been observed in patients receiving BLINCYTO®, especially in patients previously treated with cranial irradiation and anti-leukemic chemotherapy. Preparation and administration errors have occurred with BLINCYTO® treatment. Follow instructions for preparation (including admixing) and administration in the PI strictly to minimize medication errors (including underdose and overdose).

Adverse Reactions
The most commonly reported adverse reactions (≥ 20%) in clinical trials were pyrexia (62%), headache (36%), peripheral edema (25%), febrile neutropenia (25%), nausea (25%), hypokalemia (23%), rash (21%), tremor (20%), diarrhea (20%) and constipation (20%). Serious adverse reactions were reported in 65% of patients. The most common serious adverse reactions (≥ 2%) included febrile neutropenia, pyrexia, pneumonia, sepsis, neutropenia, device-related infection, tremor, encephalopathy, infection, overdose, confusion, Staphylococcal bacteremia, and headache.

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 U.S. Prescribing Information and medication guide for BLINCYTO at www.BLINCYTO.com.

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 or us) and are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially from those described. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission (SEC) reports filed by Amgen Inc., including Amgen Inc.'s most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and Form 8-K. Please refer to Amgen Inc.'s most recent Forms 10-K, 10-Q and 8-K for additional information on the uncertainties and risk factors related to our business. Unless otherwise noted, Amgen is providing this information as of Sept. 25, 2015, and expressly disclaims any duty to update information contained in this news release.

No forward-looking statement can be guaranteed and actual results may differ materially from those we project. Discovery or identification of new product candidates or development of new indications for existing products cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate or development of a new indication for an existing product will be successful and become a commercial product. Further, preclinical results do not guarantee safe and effective performance of product candidates in humans. The complexity of the human body cannot be perfectly, or sometimes, even adequately modeled by computer or cell culture systems or animal models. The length of time that it takes for us and our partners to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and we expect similar variability in the future. We develop product candidates internally and through licensing collaborations, partnerships and joint ventures. Product candidates that are derived from relationships may be subject to disputes between the parties or may prove to be not as effective or as safe as we may have believed at the time of entering into such relationship. Also, we or others could identify safety, side effects or manufacturing problems with our products after they are on the market. Our business may be impacted by government investigations, litigation and product liability claims. If we fail to meet the compliance obligations in the corporate integrity agreement between us and the U.S. government, we could become subject to significant sanctions. We depend on third parties for a significant portion of our manufacturing capacity for the supply of certain of our current and future products and limits on supply may constrain sales of certain of our current products and product candidate development.

In addition, sales of our products (including products of our wholly-owned subsidiaries) are affected by the reimbursement policies imposed by third-party payers, including governments, private insurance plans and managed care providers and may be affected by regulatory, clinical and guideline developments and domestic and international trends toward managed care and healthcare cost containment as well as U.S. legislation affecting pharmaceutical pricing and reimbursement. Government and others' regulations and reimbursement policies may affect the development, usage and pricing of our products. In addition, we compete with other companies with respect to some of our marketed products as well as for the discovery and development of new products. We believe that some of our newer products, product candidates or new indications for existing products, may face competition when and as they are approved and marketed. Our products may compete against products that have lower prices, established reimbursement, superior performance, are easier to administer, or that are otherwise competitive with our products. In addition, while Amgen and its partners routinely obtain patents for their products and technology, the protection of our products offered by patents and patent applications may be challenged, invalidated or circumvented by our or our partners' competitors and there can be no guarantee of our or our partners' ability to obtain or maintain patent protection for our products or product candidates. We cannot guarantee that we will be able to produce commercially successful products or maintain the commercial success of our existing products. Our stock price may be affected by actual or perceived market opportunity, competitive position, and success or failure of our products or product candidates. Further, the discovery of significant problems with a product similar to one of our products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on our business and results of operations. Our efforts to integrate the operations of companies we have acquired may not be successful. We may experience

difficulties, delays or unexpected costs and not achieve anticipated benefits and savings from our ongoing restructuring plan. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or their ability to pay a dividend or repurchase our common stock.

The scientific information discussed in this news release related to our product candidates is limited to the European Union. Such product candidates are not approved by the European Medicines Agency, and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidates.

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