New Analyses Presented At ASH 2015 Demonstrate The Potential Of Kyprolis® (Carfilzomib) As Backbone Therapy In Multiple Myeloma

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Data Confirm Efficacy and Safety of Kyprolis Combination Across Range of Patient Populations

THOUSAND OAKS, Calif., Dec. 5, 2015 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced the presentation of new key data evaluating Kyprolis® (carfilzomib) -based regimens in patients with relapsed multiple myeloma. The data showed Kyprolis in combination with dexamethasone significantly extended disease progression compared to bortezomib plus dexamethasone across a range of difficult-to-treat populations, specifically those with high risk and previously treated disease. The analyses were presented during the 57th Annual Meeting and Exposition of the American Society of Hematology (ASH) in Orlando, Fla.

Data analyzed in three presentations across patient subgroups from the Phase 3 ENDEAVOR trial showed that patients with relapsed or refractory multiple myeloma, who were treated with Kyprolis plus dexamethasone, achieved superior progression-free survival (PFS) compared to those receiving bortezomib plus dexamethasone. The subgroup analyses evaluated the Kyprolis combination based on prior treatment, cytogenetic risk status and age, respectively (ASH abstracts #729, #30 and #1844). Pivotal data from the Phase 3 ENDEAVOR trial were previously presented at the 2015 Annual Meeting of the American Society of Clinical Oncology (ASCO) and published online in *The Lancet Oncology* today.

A separate presentation analyzed the efficacy and safety of Kyprolis according to baseline cytogenetic risk status, based on data from the Phase 3 ASPIRE trial in which Kyprolis in combination with lenalidomide and dexamethasone demonstrated a significant improvement in PFS compared to lenalidomide and dexamethasone (ASH abstract #731).

"Our clinical research with Kyprolis aims to improve outcomes for patients in the relapsed setting, which are currently poor due to more aggressive disease biology as multiple myeloma progresses," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "This week's presentations show that even in difficult-to-treat populations, Kyprolis significantly extends the time patients can live without their disease progressing and improves the depth and duration of a response, compared to current standard of care therapies."

Multiple myeloma is characterized by very complex cytogenetic and molecular genetic aberrations.[1] Cytogenetic analysis may provide more information about myeloma prognosis and help physicians with treatment plans.[2] Myeloma cytogenetic analysis is an examination of the bone marrow cells to look for chromosome abnormalities.[2]

Abstracts are currently available on the ASH website.

ASH Abstract #729: Impact of Prior Treatment on Patients with Relapsed Multiple Myeloma Treated with Carfilzomib and Dexamethasone Versus Bortezomib and Dexamethasone in a Subgroup Analysis of the Phase 3 ENDEAVOR Study (NCT01568866)
This preplanned, exploratory sub-analysis assessed treatment with Kyprolis and dexamethasone or bortezomib and dexamethasone in 929 total patients. The proportion of patients with one prior therapy compared to those with two or more prior lines of therapy was balanced between the treatment arms. The proportion of patients with prior bortezomib or lenalidomide exposure was also balanced across treatment arms within the subgroups of patients with one or two or more prior lines of therapy. The analysis demonstrated a favorable benefit-risk profile of Kyprolis regardless of prior treatment, including number and types of prior therapy.

- Median PFS for patients after one prior line of therapy was 22.2 months (95 percent CI, 17.7–not estimable [NE]) for the Kyprolis-containing regimen versus 10.1 months (95 percent CI, 8.8–12.7) for the bortezomib-containing regimen (HR: 0.45). Median PFS for patients who had two or more previous lines of therapy was 14.9 months (10.2–NE) for Kyprolis patients compared with 8.4 months (6.5–10.2) for bortezomib patients (HR: 0.60).
- Grade 3 or higher adverse events were reported in 69.8 percent of Kyprolis patients and 63.9 percent of bortezomib patients previously treated with one prior line, and 76.6 percent of Kyprolis patients and 69.9 percent of bortezomib patients with two or more prior lines.

ASH Abstract #30: Efficacy and Safety of Carfilzomib and Dexamethasone Versus Bortezomib and Dexamethasone in Patients with Relapsed Multiple Myeloma Based on Cytogenetic Risk Status: Subgroup Analysis from the Phase 3 Study ENDEAVOR (NCT01568866)
In this preplanned, exploratory sub-analysis of the efficacy and safety of Kyprolis and dexamethasone versus bortezomib and dexamethasone based on baseline cytogenetic risk status, Kyprolis demonstrated superiority to bortezomib and a favorable benefit–risk profile, regardless of baseline cytogenetic risk status, in patients with high-risk relapsed multiple myeloma.

- Median PFS in the high-risk group (n=210) was 8.8 months (95 percent CI, 6.9–11.3) for Kyprolis patients versus 6.0 months (4.9–8.1) for bortezomib patients (HR: 0.646). Median PFS in the standard-risk group (n=575) was not estimable for Kyprolis (18.7–NE) versus 10.2 months (9.3–12.2) for bortezomib (HR: 0.439).
- Grade 3 or higher adverse events for Kyprolis compared with bortezomib, in the high- and standard-risk groups, were 70.1 percent versus 63.1 percent, and 73.9 percent versus 68.3 percent, respectively.

ASH Abstract #1844: Carfilzomib and Dexamethasone versus Bortezomib and Dexamethasone in Patients With Relapsed Multiple Myeloma: Results of the Phase 3 Study ENDEAVOR (NCT01568866) According to Age Subgroup
In this exploratory subgroup analysis from the ENDEAVOR study according to age, treatment with Kyprolis and dexamethasone demonstrated clinically meaningful improvement in PFS compared with bortezomib and dexamethasone in all age subgroups examined, with a trend toward a greater improvement in the eldest-age subgroup (75 or older) than in the two younger-age subgroups (under 65 and 65–74 years).

- Median PFS was improved with the Kyprolis regimen compared with the bortezomib regimen, within each age subgroup (under 65: NE versus 9.5 months [HR: 0.58]; 65–74 years: 15.6 months versus 9.5 months [HR: 0.53]; 75 and older: 18.7 months versus 8.9 months [HR: 0.38]).
- Selected grade 3 or higher adverse events of interest that were higher in the Kyprolis arm within each age subgroup, compared with the bortezomib arm, were hypertension, dyspnea, cardiac failure and renal failure.

ASH Abstract #731: Efficacy and Safety of Carfilzomib, Lenalidomide, and Dexamethasone Versus Lenalidomide and Dexamethasone in Patients With Relapsed Multiple Myeloma Based on Cytogenetic Risk Status: Subgroup Analysis From the Phase 3 Study ASPIRE (NCT01080391)
This preplanned, exploratory sub-analysis assessed the efficacy and safety of Kyprolis, lenalidomide and dexamethasone (KRd) compared with lenalidomide and dexamethasone (Rd) alone, in 417 patients with relapsed multiple myeloma with high- and standard-risk cytogenetic status, and found Kyprolis had a favorable benefit–risk profile, regardless of baseline cytogenetic risk status, and improved outcomes in patients with high-risk disease.

- Median PFS in the high-risk group (n=100) was 23.1 months (95 percent CI, 12.5–24.2) for the Kyprolis-containing regimen versus 13.9 months (9.5–16.7) for lenalidomide and dexamethasone alone (HR: 0.639). Median PFS in the standard-risk group (n=317) was 29.6 months (24.1–NE) for the Kyprolis-containing regimen versus 19.5 months (14.8–26.0) for the Rd regimen (HR: 0.657).
- Selected grade 3 or higher adverse events in patients treated with Kyprolis, in both cytogenetic risk groups, included dyspnea, hypertension, acute renal failure, cardiac failure, ischemic heart disease and peripheral neuropathy.

Amgen Webcast Investor Meeting
Amgen will host a webcast investor meeting at ASH on Monday, Dec. 7, 2015, at 7 p.m. ET. Sean E. Harper, M.D., executive vice president of Research and Development at Amgen, along with members of Amgen's clinical development team and clinical investigators will participate to discuss data presented at ASH and Amgen's broader oncology portfolio of products.

Live audio of the conference call will be simultaneously broadcast over the Internet and will be available to members of the news media, investors and the general public.

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

About Multiple Myeloma
Multiple myeloma is an incurable blood cancer, characterized by a recurring pattern of remission and relapse.[3] It is a rare and very aggressive orphan disease that accounts for approximately one percent of all cancers.[4-6] Worldwide, approximately 114,000 people are diagnosed with multiple myeloma each year and 80,000 patient deaths are reported on an annual basis.[4]

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

About Kyprolis® (carfilzomib) for Injection
Kyprolis® (carfilzomib) for Injection received approval from the U.S. Food and Drug Administration (FDA) in July 2015 for combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received one to three prior lines of therapy.

Kyprolis is also indicated under FDA accelerated approval in July 2012 as a single agent for the treatment of patients with multiple myeloma who have received at least two prior therapies including bortezomib and an immunomodulatory agent and have demonstrated disease progression on or within 60 days of completion of the last therapy. Approval is based on response rate. Clinical benefit, such as improvement in survival or symptoms, has not been verified.

In Nov. 2015, the European Commission granted marketing authorization for Kyprolis in combination with lenalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

Kyprolis is a product of Onyx Pharmaceuticals, Inc. Onyx Pharmaceuticals is a subsidiary of Amgen and holds development and commercialization rights to Kyprolis globally, excluding Japan. Kyprolis is also approved for use in Argentina, Israel, Kuwait, Mexico, Thailand and Colombia. Additional regulatory applications for Kyprolis are underway and have been submitted to health authorities worldwide.

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

Important Safety Information Regarding Kyprolis® (carfilzomib) for Injection

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. 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, 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 percent 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 percent 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 prescribing information is available at www.kyprolis.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, we or us) and are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially from those described. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission (SEC) reports filed by Amgen Inc., including Amgen Inc.'s most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and Form 8-K. Please refer to Amgen Inc.'s most recent Forms 10-K, 10-Q and 8-K for additional information on the uncertainties and risk factors related to Amgen's business. Unless otherwise noted, Amgen is providing this information as of Dec. 5, 2015, and expressly disclaims any duty to update information contained in this news release.

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

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

The scientific information discussed in this news release relating to new indications for Amgen's products is preliminary and investigative and is not part of the labeling approved by the U.S. Food and Drug Administration for the products. The products are not approved for the investigational use(s) discussed in this news release and no conclusions can or should be drawn regarding the safety or effectiveness of the products for these uses.

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