FDA Grants Priority Review for Amgen's Supplemental New Drug Application for Expanded Labeling of Kyprolis® (Carfilzomib) in Relapsed Multiple Myeloma

September 18, 2015

Application Based on Phase 3 Head-to-Head Trial Showing Superiority of Kyprolis and Dexamethasone Over Bortezomib Plus Dexamethasone

THOUSAND OAKS, Calif., Sept. 18, 2015 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced the U.S. Food and Drug Administration (FDA) has accepted for priority review the supplemental New Drug Application (sNDA) of Kyprolis® (carfilzomib) for Injection for patients with relapsed multiple myeloma. The sNDA is designed to expand the current indication to include Kyprolis in combination with dexamethasone for patients who have received at least one prior therapy. The Prescription Drug User Fee Act (PDUFA) target action date is Jan. 22, 2016.

The FDA's acceptance of this new sNDA for Kyprolis follows the recent FDA approval for Kyprolis in combination with Revlimid® (lenalidomide) and dexamethasone for the treatment of patients with relapsed multiple myeloma who have received one to three prior lines of therapy.

Multiple myeloma is a rare and complex blood cancer that has historically been one of the most difficult to treat diseases because of the inherent complexities related to the recurring pattern of remission and relapse. Patients face poor outcomes, which worsen with each relapse.

"Clinicians need a range of options and robust clinical data to make informed choices that can ideally extend the time patients live without their cancer progressing," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "The acceptance of this submission is an important next step toward providing more options for patients with relapsed multiple myeloma and we look forward to working with the FDA over the coming months."

The application is based on data from the Phase 3 head-to-head ENDEAVOR study, which showed that patients with relapsed multiple myeloma treated with Kyprolis and low-dose dexamethasone lived twice as long without their disease worsening, demonstrating statistically and clinically significant superiority over bortezomib and low-dose dexamethasone (median progression-free survival [PFS] 18.7 months versus 9.4 months, HR=0.53, 95 percent CI, 0.44 – 0.65; p<0.0001).

Treatment discontinuation due to adverse events and on-study deaths was comparable between the two arms. The rates of cardiac failure and renal failure for Kyprolis were comparable to those observed in the Phase 3 ASPIRE study. In ENDEAVOR, the rates for cardiac and renal failure were higher in the Kyprolis arm versus the bortezomib arm. There was also an increase in the incidence of hypertension and dyspnea in the Kyprolis arm compared to bortezomib in ENDEAVOR.

Priority review is assigned to applications for drugs that treat serious conditions and would, if approved, provide significant improvements in the safety or effectiveness of the treatment, diagnosis or prevention of serious conditions.

About ENDEAVOR

The randomized ENDEAVOR (Randomiz**E**d, Ope**N** Label, Phase 3 Study of Carfilzomib Plus **DE**xameth**A**sone **V**s Bortezomib Plus Dexamethas**O**ne in Patients With **R**elapsed Multiple Myeloma) trial of 929 patients evaluated Kyprolis in combination with low-dose dexamethasone, versus bortezomib with low-dose dexamethasone in patients whose multiple myeloma has relapsed after at least one, but not more than three prior therapeutic regimens. The primary endpoint of the trial was PFS, defined as the time from treatment initiation to disease progression or death.

Patients received Kyprolis as a 30-minute infusion on two consecutive days, each week for three weeks followed by a 12 day rest period. Kyprolis was administered on days 1, 2, 8, 9, 15 and 16 of 28 day treatment cycles, along with low-dose dexamethasone (20 mg). For Cycle 1 only, Kyprolis was administered at 20 mg/m^2 on days 1 and 2, followed by escalation to 56 mg/m^2 from day 8. Patients who tolerated 56 mg/m^2 in Cycle 1 were kept at this dose for subsequent cycles. Patients who received bortezomib (1.3 mg/m^2) with low-dose dexamethasone (20 mg) were administered bortezomib subcutaneously or intravenously at the discretion of the investigator and in accordance with regulatory approval of bortezomib. More than 75 percent of the patients in the control arm received bortezomib subcutaneously. This study was conducted at 235 sites worldwide. For information about this trial, please visit www.clinicaltrials.gov under trial identification number NCT01568866.

About Multiple Myeloma

Multiple myeloma is the second most common hematologic cancer and results from an abnormality of plasma cells, usually in the bone marrow.[1,2] Worldwide, nearly 230,000 people are living with multiple myeloma and approximately 114,000 new cases are diagnosed annually.[3] In the U.S., there are nearly 96,000 people living with, or in remission from, multiple myeloma. The estimated number of new cases of multiple myeloma in 2014 was more than 24,000 in the U.S. and the estimated number of deaths was 11,090.[4] In Europe, approximately 89,000 people are living with the disease and in 2012 there was an estimated 39,000 newly diagnosed cases and 24,000 deaths.[3]

About Kyprolis® (carfilzomib) for Injection

Kyprolis® (carfilzomib) for Injection received approval from the U.S. 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.

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

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% 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 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) and are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially from those described. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission (SEC) reports filed by Amgen Inc., including Amgen Inc.'s most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and Form 8-K. Please refer to Amgen Inc.'s most recent Forms 10-K, 10-Q and 8-K for additional information on the uncertainties and risk factors related to Amgen's business. Unless otherwise noted, Amgen is providing this information as of Sept. 18, 2015 and expressly disclaims any duty to update information contained in this news release.

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

In addition, sales of Amgen's products (including products of Amgen's wholly-owned subsidiaries) are affected by the reimbursement policies imposed by third-party payers, including governments, private insurance plans and managed care providers and may be affected by regulatory, clinical and guideline developments and domestic and international trends toward managed care and healthcare cost containment as well as U.S. legislation affecting pharmaceutical pricing and reimbursement. Government and others' regulations and reimbursement policies may affect the development, usage and pricing of Amgen's products. In addition, Amgen competes with other companies with respect to some of its marketed products as well as

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

The scientific information discussed in this news release 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.

Kyprolis® is a registered trademark of Onyx Pharmaceuticals, Inc., an Amgen Inc. subsidiary.

Revlimid® is registered trademark of Celgene Corporation.

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