July 27, 2015

FDA Approves Kyprolis® (carfilzomib) For Combination Use In The Treatment Of Patients With Relapsed Multiple Myeloma

THOUSAND OAKS, Calif.(July 24, 2015) -- Amgen (NASDAQ:AMGN) announced that the U.S. Food and Drug Administration (FDA) approved the supplemental New Drug Application (sNDA) for Kyprolis® (carfilzomib) for Injection in combination with Revlimid® (lenalidomide) and dexamethasone (KRd) for the treatment of patients with multiple myeloma who have received one to three prior lines of therapy.

Attached is the press release distributed by Amgen for your information.

In Japan, ONO entered into an exclusive license agreement with Onyx, a subsidiary of Amgen, in September 2010 to develop and commercialize two compounds from Onyx's proteasome inhibitor development program, carfilzomib (for injection) and oprozomib (orally administered) for all oncology indications. ONO is conducting some clinical trials of carfilzomib（ONO-7057）in patients with multiple myeloma.

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News Release

FDA Approves Kyprolis® (carfilzomib) For Combination Use In The Treatment Of Patients With Relapsed Multiple Myeloma

Approval Expands Kyprolis Indication
Patients Treated With Kyprolis in Combination With Standard of Care Lived 50 Percent Longer Without Disease Worsening Compared to Standard of Care Alone in Pivotal Study

THOUSAND OAKS, Calif. (July 24, 2015) -- Amgen (NASDAQ:AMGN) today announced that the U.S. Food and Drug Administration (FDA) approved the supplemental New Drug Application (sNDA) for Kyprolis® (carfilzomib) for Injection in combination with Revlimid® (lenalidomide) and dexamethasone (KRd) for the treatment of patients with multiple myeloma who have received one to three prior lines of therapy.

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"The expanded indication of Kyprolis provides patients with relapsed multiple myeloma a new therapeutic option, helping to address a real unmet need for this common blood cancer," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "The approval of a second indication for Kyprolis in just three years demonstrates that it is becoming a critical component in the treatment of multiple myeloma, and underscores our commitment to advancing care for patients with this challenging disease."

The FDA approved the expanded indication for Kyprolis based on data from the ASPIRE study. The study showed that patients treated in the KRd arm lived 50 percent longer (8.7 months) without their disease worsening compared to patients treated with Revlimid and low-dose dexamethasone (Rd) alone. The median progression-free survival (PFS) was 26.3 months (95 percent CI, 23.3 to 30.5 months) in the KRd arm compared to 17.6 months (95 percent CI, 15.0 to 20.6 months) in the Rd arm. The most common adverse events in the Kyprolis arm included pneumonia (1 percent), myocardial infarction (0.8 percent) and upper respiratory tract infection (0.8 percent).

"The ability of this Kyprolis treatment regimen to produce deep and durable responses is critical towards extending the time patients live without their disease progressing," said ASPIRE principal investigator Keith Stewart, M.D., Ch.B.

Additional regulatory applications for Kyprolis are underway and have been submitted to health authorities worldwide.

Multiple myeloma is the second most common hematologic cancer.[1] In the U.S., there are nearly 96,000 people living with, or in remission from, multiple myeloma.[2] The estimated number of new cases of multiple myeloma in 2014 was more than 24,000 and the estimated number of deaths was 11,090.[2]

About ASPIRE

The international, randomized 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 evaluated Kyprolis in combination with lenalidomide and low-dose dexamethasone, versus lenalidomide and low-dose dexamethasone alone, in patients with relapsed multiple myeloma following treatment with one to three prior regimens. The primary endpoint of the trial was PFS, defined as the time from treatment initiation to disease progression or death. 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 on days 8, 9, 15 and 16 of cycle one and continuing on days 1, 2, 8, 9, 15 and 16 of subsequent cycles), in addition to a standard dosing schedule of lenalidomide (25 mg per day for 21 days on, 7 days off) and low-dose dexamethasone (40 mg per week in four-week cycles), versus lenalidomide and low-dose dexamethasone alone. The study randomized 792 patients at sites in North America, Europe and Israel.

The OS results did not cross the pre-specified early stopping boundary for the interim analysis. At the time of the interim analysis, there were 143 deaths (36.1 percent) in the KRd group, compared to 162 deaths (40.9 percent) in the Rd group. The ORR was 87 percent with KRd and 67 percent with Rd. In the KRd and Rd groups, 14 percent versus 4 percent of patients achieved a stringent complete response, a measurement indicating depth of response. 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).

The rate of deaths due to adverse events (AEs) within 30 days of the last dose was balanced between the KRd arm and the Rd arm. The most common causes of death 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 1.5 percent), pyrexia (4 percent versus 2 percent), and pulmonary embolism (3 percent versus 2 percent). Discontinuation due to any AE occurred in 26 percent of patients in the KRd arm versus 25 percent of patients in the Rd arm. Adverse events leading to discontinuation of Kyprolis occurred in 12 percent of patients.

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.

About Kyprolis® (carfilzomib) for Injection

Kyprolis® (carfilzomib) for Injection is indicated in 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 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, Mexico and Thailand. For more information about Kyprolis, visit **www.kyprolis.com**.

Important Safety Information Regarding Kyprolis® (carfilzomib) for Injection

WARNINGS AND PRECAUTIONS

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. In clinical studies with Kyprolis, these events typically occurred early in the course of Kyprolis therapy (< 5 cycles). 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 at 1 dose level reduction based on a benefit/risk assessment. While adequate hydration is required prior to each dose in Cycle 1, all patients should also be monitored 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. In patients ≥ 75 years of age, 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 uncontrolled by medications were not eligible for the clinical trials. These patients may be at greater risk for cardiac complications.

Acute Renal Failure:

Cases of acute renal failure have occurred in patients receiving Kyprolis. Renal insufficiency adverse events (renal impairment, acute renal failure, renal failure) have occurred with an incidence of approximately 8% in a randomized controlled trial. 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 (calculated using Cockcroft and Gault equation). 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 been reported in patients who received Kyprolis. Patients with multiple myeloma and a high tumor burden should be considered to be at greater risk for TLS. Ensure that patients are well hydrated before administration of Kyprolis 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 including interruption of 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 less than 1% of 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 approximately 1% of patients treated with Kyprolis and was Grade 3 or greater in less than 1% of patients. Evaluate with cardiac imaging and/or other tests as indicated. Withhold Kyprolis for pulmonary 11 hypertension until resolved or returned to baseline and consider whether to restart Kyprolis based on a benefit/risk assessment.

Dyspnea:
Dyspnea was reported in 28% of patients treated with Kyprolis and was Grade 3 or greater in 4% of patients. 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. In the combination study, the incidence of venous thromboembolic events in the first 12 cycles was 13% in the Kyprolis combination arm versus 6% in the control arm. With Kyprolis monotherapy, the incidence of venous thromboembolic events was 2%. 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. Administer dexamethasone prior to Kyprolis to reduce the incidence and severity 12 of infusion reactions. Inform patients of the risk and of symptoms and to contact a physician immediately if symptoms of an infusion reaction occur.

Thrombocytopenia:
Kyprolis causes thrombocytopenia with platelet nadirs observed between Day 8 and Day 15 of each 28-day cycle with recovery to baseline platelet count usually by the start of the next cycle. Thrombocytopenia was reported in approximately 40% of patients in clinical trials with 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 (< 1%) 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:
Cases of thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS) including fatal outcome have been reported in patients who received Kyprolis. Monitor for signs and symptoms of TTP/HUS. If the diagnosis is suspected, stop Kyprolis and evaluate. 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 been reported in patients receiving Kyprolis. Posterior reversible encephalopathy syndrome (PRES), formerly termed Reversible Posterior Leukoencephalopathy Syndrome (RPLS), is a neurological disorder which can present with seizure, headache, lethargy, confusion, blindness, altered consciousness, and other visual and neurological disturbances, along with hypertension, and the diagnosis is confirmed by neuro-radiological imaging (MRI). 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. There are no adequate and well-controlled studies in pregnant women using Kyprolis. Kyprolis caused embryo-fetal toxicity in pregnant rabbits at doses that were lower than in patients receiving the recommended dose. Females of reproductive potential should be advised to avoid becoming pregnant while being treated with Kyprolis. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

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.

USE IN SPECIFIC POPULATIONS

Patients on dialysis: Administer Kyprolis after the dialysis procedure.

POST-MARKETING EXPERIENCE

The following adverse reactions were reported in the post-marketing experience: dehydration, thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS), tumor lysis syndrome including fatal outcomes, and posterior reversible encephalopathy syndrome (PRES). Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

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 July 24, 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 recently announced 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.

1. **Dimopoulos, MA and Terpos E. Multiple Myeloma. *Annals of Oncology* 21 (Supplement 7): vii143–vii150, 2010.**

2. **Leukemia & Lymphoma Society. Facts 2014-2015. Available at: http://www.lls.org/content/nationalcontent/resourcecenter/freeeducationmaterials/generalcancer/pdf/facts.pdf Accessed July 2015.**

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