



Amgen Submits Supplemental New Drug Application For Kyprolis® (Carfilzomib) In Relapsed Multiple Myeloma

July 23, 2015

Filing Based on Data From Phase 3 Head-To-Head ENDEAVOR Study

Relapsed Multiple Myeloma Patients Treated With Kyprolis in Study Lived Twice as Long Without Disease Worsening

THOUSAND OAKS, Calif., July 23, 2015 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced the submission of a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) for Kyprolis® (carfilzomib) for Injection to seek an expanded indication for the treatment of patients with a form of blood cancer, relapsed multiple myeloma, who have received at least one prior therapy. Kyprolis currently has accelerated approval in the U.S. for the treatment of patients with relapsed multiple myeloma as a monotherapy.

The sNDA is based on data from the global Phase 3 ENDEAVOR trial. The ENDEAVOR study is the first of two head-to-head Phase 3 trials of Kyprolis versus Velcade® (bortezomib). Relapsed multiple myeloma patients treated with Kyprolis and dexamethasone in the ENDEAVOR study lived twice as long without their disease worsening, demonstrating statistically and clinically significant superiority over Velcade (median progression-free survival [PFS] 18.7 months versus 9.4 months, HR=0.53, 95 percent CI, 0.44 – 0.65; $p < 0.0001$).

"Submission of this new sNDA for Kyprolis is important because if approved, it will mean more treatment options for patients with this serious disease. Multiple myeloma 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," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "The ENDEAVOR study showed that patients who had failed at least one prior therapy were half as likely to see their disease worsen if they received Kyprolis. This is yet another data set that illustrates Kyprolis' potential to extend the time patients live without their disease progressing and improve the depth and duration of a response."

The Kyprolis combination demonstrated superiority over the Velcade combination for secondary objectives of higher overall response rate and lower neuropathy events. Overall survival data are not yet mature and continue to be monitored.

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 Velcade arm. There was also an increase in the incidence of hypertension and dyspnea in the Kyprolis arm compared to Velcade in ENDEAVOR and than that observed in the ASPIRE study.

Based on the Phase 3 ASPIRE study Amgen continues to work with the FDA on the related sNDA in the U.S. and with the European Union (EU) regulatory authorities for the Marketing Authorization Application for Kyprolis. Following potential approval based on the ASPIRE study, Amgen plans to submit ENDEAVOR for potential authorization in the EU.

Kyprolis Head-to-Head Studies

The randomized ENDEAVOR (Randomized, Open-Label, Phase 3 Study of Carfilzomib Plus Dexamethasone Versus Bortezomib Plus Dexamethasone in Patients With Relapsed Multiple Myeloma) trial of 929 patients evaluated Kyprolis in combination with dexamethasone, versus Velcade with 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 along with dexamethasone (20 mg). Administer Kyprolis at a starting dose of 20 mg/m² in Cycle 1 on Days 1 and 2. If tolerated, escalate the dose to a target dose of 56 mg/m² on Day 8 of Cycle 1. Patients were kept at 56 mg/m² on days 9, 15 and 16 on a 28 day cycle. Patients who tolerated 56 mg/m² in Cycle 1 were kept at this dose for subsequent cycles on days 1, 2, 8, 9, 15 and 16 on a 28 day cycle. Patients who received Velcade (1.3 mg/m²) with dexamethasone (20 mg) were administered Velcade subcutaneously or intravenously at the discretion of the investigator and in accordance with regulatory approval of Velcade. More than 75 percent of the patients in the control arm received Velcade subcutaneously. This study was conducted at 235 sites worldwide. For information about this trial, please visit www.clinicaltrials.gov under trial identification number NCT01568866.

Kyprolis is also being evaluated in the CLARION study, a head-to-head Phase 3 multicenter, open-label, randomized study in transplant-ineligible patients with newly diagnosed multiple myeloma. The study is evaluating the safety and efficacy of carfilzomib, melphalan and prednisone versus bortezomib, melphalan and prednisone. For information about this trial, please visit www.clinicaltrials.gov under trial identification number NCT01818752.

About Multiple Myeloma

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 Kyprolis® (carfilzomib) for Injection

Kyprolis® (carfilzomib) for Injection is indicated 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

This safety information is specific to the current U.S. approved indication, which is based on Phase 2 studies.

Safety data have been evaluated in 526 patients with relapsed and/or refractory multiple myeloma who received single-agent Kyprolis. There were 37 deaths in the Phase 2 studies, or 7 percent of patients. The most common causes of death, other than disease progression, were cardiac (5 patients), end-organ failure (4 patients) and infection (4 patients). Important warnings and precautions include cardiac arrest, congestive heart failure, myocardial ischemia, pulmonary hypertension, pulmonary complications, infusion reactions, tumor lysis syndrome, thrombocytopenia, hepatic toxicity and embryo-fetal toxicity.

Death due to cardiac arrest has occurred within a day of Kyprolis administration. Patients with New York Heart Association Class III and IV heart failure, myocardial infarction in the preceding 6 months and conduction abnormalities uncontrolled by medications were not eligible for the clinical trials. These patients may be at greater risk for cardiac complications.

Pulmonary arterial hypertension (PAH) was reported in 2 percent of patients treated with Kyprolis and was Grade 3 or greater in less than 1 percent of patients. Dyspnea was reported in 35 percent of patients enrolled in clinical trials. Grade 3 dyspnea occurred in 5 percent; no Grade 4 events and 1 death (Grade 5) was reported.

Infusion reactions, characterized by a spectrum of systemic symptoms including fever, chills, arthralgia, myalgia, facial flushing, facial edema, vomiting, weakness, shortness of breath, hypotension, syncope, chest tightness, or angina can occur immediately following or up to 24 hours after administration of Kyprolis. Administration of dexamethasone prior to Kyprolis reduces the incidence and severity of reactions. Tumor lysis syndrome (TLS) occurred following Kyprolis administration in <1 percent of patients. Patients with multiple myeloma and a high tumor burden should be considered to be at greater risk for TLS.

Thrombocytopenia following Kyprolis administration resulted in a dose reduction in 1 percent of patients and discontinuation of treatment with Kyprolis in <1 percent of patients.

Cases of hepatic failure, including fatal cases, have been reported (<1 percent). Kyprolis can cause elevations of serum transaminases and bilirubin.

Cases of thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS) including fatal outcome have been reported. Treatment with Kyprolis should be discontinued if signs and symptoms of TTP/HUS occur.

Cases of posterior reversible encephalopathy syndrome (PRES) have been reported. Treatment with Kyprolis should be discontinued if PRES is suspected.

There are no adequate and well-controlled studies in pregnant women using Kyprolis. Females of reproductive potential should be advised to avoid becoming pregnant while being treated with Kyprolis.

The most common serious adverse reactions were pneumonia, acute renal failure, pyrexia and congestive heart failure. The most common adverse reactions (incidence of 30 percent or greater) observed in clinical trials of patients with multiple myeloma were fatigue, anemia, nausea, thrombocytopenia, dyspnea, diarrhea and pyrexia. Serious adverse reactions were reported in 45 percent of patients.

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 23, 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.

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.

CONTACT: Amgen, Thousand Oaks
Kristen Davis, 805-447-3008 (media)
Trish Hawkins, 805-447-5631 (media)
Arvind Sood, 805-447-1060 (Investors)

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.



Logo - <http://photos.prnewswire.com/prnh/20081015/AMGENLOGO>

To view the original version on PR Newswire, visit: <http://www.prnewswire.com/news-releases/amgen-submits-supplemental-new-drug-application-for-kyprolis-carfilzomib-in-relapsed-multiple-myeloma-300117605.html>

SOURCE Amgen