



## Amgen Announces Top-Line Results From Phase 3 Focus Trial Of Kyprolis® In Patients With Relapsed And Advanced Refractory Multiple Myeloma

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THOUSAND OAKS, Calif. and SOUTH SAN FRANCISCO, Calif., Aug. 13, 2014 /PRNewswire/ -- Amgen (NASDAQ:AMGN) and its subsidiary, Onyx Pharmaceuticals, Inc., today announced that the Phase 3 clinical trial FOCUS (CarFilzOmib for AdvanCed Refractory MUltiple Myeloma European Study) did not meet its primary endpoint of improving overall survival (OS) (HR=0.975, 95 percent CI, 0.760, 1.249). The 315-patient, open-label study evaluated single-agent Kyprolis® (carfilzomib) for Injection compared to an active control regimen of low-dose dexamethasone, or equivalent corticosteroids, plus optional cyclophosphamide in patients with relapsed and advanced refractory multiple myeloma. Nearly all patients in the control arm received cyclophosphamide. Patients were heavily pretreated and had received a median of five therapeutic regimens prior to study entry.

Treatment discontinuation due to adverse events and on-study deaths were comparable between the two arms. The rate of cardiac events observed in the Kyprolis arm was consistent with the current U.S. Kyprolis label. There was an increase in the incidence of renal adverse events of all grades observed in the Kyprolis arm compared to the active control arm and the label.

"While it is unfortunate that the FOCUS study did not meet its primary endpoint of overall survival, we believe the results from the recent positive ASPIRE Phase 3 clinical trial will be sufficient to support regulatory submissions around the world," said Pablo J. Cagnoni, M.D., president, Onyx Pharmaceuticals, Inc.

Detailed results will be submitted for presentation at an upcoming scientific meeting.

### About FOCUS

The randomized, open-label Phase 3 FOCUS (CarFilzOmib for AdvanCed Refractory MUltiple Myeloma European Study) trial evaluated single-agent Kyprolis versus an active control regimen of low-dose steroids plus optional cyclophosphamide in patients with relapsed and advanced refractory multiple myeloma following treatment with at least three prior therapies. The primary endpoint of the trial was overall survival. Secondary endpoints included progression-free survival, overall response rate, clinical benefit rate, duration of response and safety. Patients were randomized to receive Kyprolis (20mg/m<sup>2</sup> on days 1 and 2 of cycle 1 followed by 27mg/m<sup>2</sup> on days 8, 9, 15, and 16 of cycle 1 and all doses cycle 2 through 9, and 27 mg/m<sup>2</sup> on days 1,2,15, and 16 of cycle 10 and beyond) or an active control regimen of oral steroids and optional cyclophosphamide. The trial enrolled 315 patients.

### 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. In the U.S., approximately 70,000 people are living with multiple myeloma and approximately 24,000 new cases are diagnosed annually.[1] Worldwide, nearly 230,000 people are living with multiple myeloma and approximately 114,000 new cases are diagnosed annually.[2] In Europe, approximately 89,000 people are living with multiple myeloma, and approximately 39,000 new cases are diagnosed annually.[3]

### About Kyprolis® (carfilzomib) for Injection

On July 20, 2012, the FDA granted accelerated approval of Kyprolis® (carfilzomib) for Injection for the treatment of patients with multiple myeloma who have received at least two prior therapies including bortezomib and an immunomodulatory agent (IMiD), and have demonstrated disease progression on or within 60 days of completion of the last therapy. Approval was based on response rate. Clinical benefit, such as improvement in survival or symptoms, has not been verified.

Kyprolis is marketed in the U.S. by Onyx Pharmaceuticals, Inc., an Amgen subsidiary.

### Important Safety Information Regarding Kyprolis® (carfilzomib) for Injection

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% 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% of patients treated with Kyprolis and was Grade 3 or greater in less than 1% of patients. Dyspnea was reported in 35% of patients enrolled in clinical trials. Grade 3 dyspnea occurred in 5%; 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% 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% of patients and discontinuation of treatment with Kyprolis in < 1% of patients.

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

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% 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% of patients.

Full prescribing information is available at [www.kyprolis.com](http://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 the world's largest independent biotechnology company, 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](http://www.amgen.com) and follow us on [www.twitter.com/amgen](http://www.twitter.com/amgen).

#### **About Onyx Pharmaceuticals, Inc.**

Based in South San Francisco, California, Onyx Pharmaceuticals, Inc., an Amgen subsidiary, is a global biopharmaceutical company engaged in the development and commercialization of innovative therapies for improving the lives of people with cancer. The company is focused on developing novel medicines that target key molecular pathways. For more information about Onyx, visit the company's website at [www.onyx.com](http://www.onyx.com). Onyx Pharmaceuticals is on Twitter. Sign up to follow our Twitter feed @OnyxPharm at <http://twitter.com/OnyxPharm>.

#### **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 Aug. 13, 2014 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 material 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. Cost saving initiatives may result in Amgen incurring impairment or other related charges on its assets. We may experience difficulties, delays or unexpected costs and not achieve anticipated benefits and savings our recently announced restructuring plans. 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 (FDA) 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 (Amgen media)  
Danielle Bertrand, 650-266-2114 (Onyx media)  
Arvind Sood, 805-447-1060 (investors)

[1] National Cancer Institute. SEER Stat Fact Sheets: Myeloma. Available at <http://seer.cancer.gov/statfacts/html/mulmy.html>.

[2] International Agency for Research on Cancer, GLOBOCAN 2012 database. Available at <http://globocan.iarc.fr/>.

[3] Cancer Research UK. "Myeloma Incidence Statistics." Available at: <http://www.cancerresearchuk.org/cancer-info/cancerstats/types/myeloma/incidence/uk-multiple-myeloma-incidence-statistics#europeandworldwide>.



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