Amgen And Onyx Announce Detailed Results From Phase 3 ASPIRE Study Of Kyprolis® (Carfilzomib) In Patients With Relapsed Multiple Myeloma

December 6, 2014

Data From Pivotal Trial Published in the New England Journal of Medicine and Presented at the 56th American Society of Hematology (ASH) Annual Meeting and Exposition

Overall Response Rate, Duration of Response, Health-Related Quality of Life Secondary Endpoints Met; Overall Survival Continues to be Monitored

Results to be Presented During an Oral Session at ASH on Sunday, December 7 at 12 p.m. PT

Data to be Featured in ASH Press Briefing on Saturday, December 6 at 8 a.m. PT

THOUSAND OAKS, Calif. and SOUTH SAN FRANCISCO, Calif., Dec. 6, 2014 /PRNewswire/ -- Amgen (NASDAQ: AMGN) and its subsidiary Onyx Pharmaceuticals, Inc., announced today results of the 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, which evaluated Kyprolis® (carfilzomib) for Injection plus Revlimid® (lenalidomide) and dexamethasone (KRd) compared with Revlimid and dexamethasone (Rd) in patients with relapsed multiple myeloma. As previously reported, the ASPIRE study met its primary endpoint by demonstrating that KRd significantly extended the time patients lived without their disease worsening, or progression-free survival (PFS), by 26.3 months compared to 17.6 months with Rd (HR=0.69; 95 percent CI: 0.57-0.83; *p*<0.0001), an 8.7 month improvement in PFS.

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The results from ASPIRE (abstract 79) will be featured during the 56th American Society of Hematology (ASH) Annual Meeting **and Exposition** press briefing on Saturday, December 6 at 8 a.m. PT and were published in the *New England Journal of Medicine*. Keith Stewart, M.B., Ch.B., dean for research at Mayo Clinic in Arizona and principal investigator will present these results in an oral session at ASH on Sunday, December 7 at 12 p.m. PT.

Secondary endpoints, which are being presented for the first time, included overall survival (OS), overall response rate (ORR), duration of response (DOR), health-related quality of life (HR-QoL) measures and safety. While the data for median OS are not yet mature based on the prespecified statistical boundary at the interim (*p*=0.005), the analysis showed a trend in favor of KRd compared with Rd (HR=0.79; 95 percent CI: 0.63-0.99; one-sided *p*=0.018, two-sided *p*=0.04). Patients will continue to be monitored for OS. The ORR was 87.1 percent with KRd and 66.7 percent with Rd (one-sided *p*<0.0001, two-sided *p*<0.001). In the KRd and Rd groups, 14 percent versus 4.3 percent of patients achieved a stringent complete response, a measurement indicating superior depth of response. Median DOR was 28.6 months (KRd) and 21.2 months (Rd). KRd consistently improved Global HR-QoL compared with Rd over 18 cycles of treatment (one-sided *p*=0.0001, two-sided *p*<0.001).

"Nearly all patients with multiple myeloma experience a relapse following treatment, underscoring the need for new options that not only extend the time patients live without their disease progressing, but also improve the depth and duration of a response to treatment," said Dr. Stewart. "The combination of carfilzomib, lenalidomide and low-dose dexamethasone generates deep and durable responses, provides a clinically meaningful improvement in progression-free survival and promises to be an important advancement in the treatment of myeloma."

Treatment discontinuation due to an adverse event (AE) occurred in 15.3 percent (KRd) versus 17.7 percent (Rd) of patients. In the KRd arm, 7.7 percent versus 8.5 percent (Rd) of patients died while still on study treatment or within 30 days of receiving the last dose of study treatment. The most common hematologic treatment-emergent AEs (≥grade 3) included neutropenia (29.6 percent [KRd] versus 26.5 percent [Rd]), anemia (17.9 percent [KRd] versus 17.2 percent [Rd]) and thrombocytopenia (16.6 percent [KRd] versus 12.3 percent [Rd]). The most common nonhematologic treatment-emergent AEs (≥grade 3) included hypokalemia (9.4 percent [KRd] versus 4.9 percent [Rd]), fatigue (7.7 percent [KRd] versus 6.4 percent [Rd]) and diarrhea (3.8 percent [KRd] versus 4.1 percent [Rd]). Other treatment-emergent AEs of interest (all grade) included dyspnea (19.4 percent [KRd] versus 14.9 percent [Rd]), hypertension (14.3 percent [KRd] versus 6.9 percent [Rd]), acute renal failure (grouped term: 8.4 percent [KRd] versus 7.2 percent [Rd]), cardiac failure (grouped term: 6.4 percent [KRd] versus 4.1 percent [Rd]) and ischemic heart disease (5.9 percent [KRd] versus 4.6 percent [Rd]). Lastly, rates of peripheral neuropathy (grouped term) were 17.1 percent (KRd) and 17.0 percent (Rd), respectively.

"Delivering new potential treatment options exemplifies Onyx and Amgen's commitment to advancing the care of patients with multiple myeloma," said Pablo J. Cagnoni, M.D., president, Onyx Pharmaceuticals, Inc. "The results from the Phase 3 ASPIRE study bring us one step closer to establishing Kyprolis as a backbone of therapy in the treatment of multiple myeloma."

Results from the ASPIRE trial will form the basis for regulatory submissions throughout the world beginning in the first half of 2015. In the U.S., the data may support the conversion of accelerated approval to full approval and expand the current indication.

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 OS, ORR, DOR, disease control rate, duration of disease control, change over time in HR-QoL and safety. Patients were randomized to receive Kyprolis (20 mg/m^2 on days 1 and 2 of cycle 1 only, then 27 mg/m^2 subsequently), 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 4 week cycles), versus lenalidomide and low-dose dexamethasone alone. In the Kyprolis arm, patients were given a 10 minute infusion on days 1, 2, 8, 9, 15 and 16. Kyprolis was omitted on days 8 and 9 during cycles 13-18 and not administered beyond 18 cycles. The study randomized 792 patients at sites in North America, Europe and Israel.

Onyx conducted the ASPIRE trial under a Special Protocol Assessment (SPA) from the U.S. Food and Drug Administration (FDA) and has received Scientific Advice from the European Medicines Agency (EMA) on the design and planned analysis of the study.

Amgen Webcast Investor Meeting
Amgen will host a webcast investor meeting on Monday, December 8, at 12 p.m. PT. Sean E. Harper, M.D., executive vice president of Research and Development at Amgen, and Pablo J. Cagnoni, M.D., president of Onyx Pharmaceuticals Inc., along with members of Amgen's clinical development team and clinical investigators, will participate in the investor meeting to discuss data presented at ASH, including the results of the pivotal Kyprolis ASPIRE study and BLINCYTO™ (blinatumomab) studies in acute lymphoblastic leukemia and diffuse large B-cell lymphoma.

Live audio of the investor meeting 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 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 U.S. 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.

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

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 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.

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 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 and follow us on 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. Onyx Pharmaceuticals is on Twitter. Sign up to follow our Twitter feed @OnyxPharm at http://twitter.com/OnyxPharm.

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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 Dec. 6, 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 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. Cost saving initiatives may result in Amgen incurring impairment or other related charges on its assets. Amgen may experience difficulties, delays or unexpected costs and not achieve anticipated cost savings from its 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.

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To view the original version on PR Newswire, visit:http://www.prnewswire.com/news-releases/amgen-and-onyx-announce-detailed-results-from-phase-3-aspire-study-of-kyprolis-carfilzomib-in-patients-with-relapsed-multiple-myeloma-300005807.html

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