U.S. FDA Approves NEXAVAR® (sorafenib) for the Treatment of Patients with Locally Recurrent or Metastatic, Progressive, Differentiated Thyroid Carcinoma Refractory to Radioactive Iodine Treatment

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First and only FDA-approved treatment option for patients with this type of thyroid cancer

WHIPPANY, N.J., THOUSAND OAKS, Calif. and SOUTH SAN FRANCISCO, Calif., Nov. 22, 2013 /PRNewswire/ -- Bayer HealthCare and Onyx Pharmaceuticals, Inc., an Amgen subsidiary (Nasdaq:AMGN), today announced that the U.S. Food and Drug Administration (FDA) has approved a supplemental New Drug Application for the oral multi-kinase inhibitor NEXAVAR® (sorafenib) tablets for the treatment of patients with locally recurrent or metastatic, progressive, differentiated thyroid carcinoma (DTC) refractory to radioactive iodine treatment. NEXAVAR was approved following a priority review by the FDA, a designation reserved for drugs that may offer a significant improvement in treatment over existing options.

(Logo: http://photos.prnewswire.com/prnh/20131122/NY22866LOGO)

"Locally recurrent or metastatic, progressive, differentiated thyroid carcinoma that is refractory to radioactive iodine treatment is difficult to treat," said Pamela A. Cyrus, M.D., Vice President and Head of U.S. Medical Affairs, Bayer HealthCare Pharmaceuticals. "NEXAVAR is the first and only FDA-approved therapy for this type of thyroid cancer and is a positive development for patients who previously had limited treatment options."

"We are pleased to be able to offer NEXAVAR as a treatment option for patients with thyroid cancer who are no longer responding to standard therapy," said Pablo J. Cagnoni, M.D., President, Onyx Pharmaceuticals, Inc. "We are committed to making this treatment available to physicians and their patients as quickly as possible."

"An unmet medical need exists for this type of thyroid cancer, underscoring the need for new therapies," said Gary Bloom, Executive Director of ThyCa: Thyroid Cancer Survivors' Association, Inc. "We are excited that an FDA-approved treatment is now available to patients coping with this challenging type of thyroid cancer."

DECISION Trial

The FDA approval is based on the results of the DECISION (stu**D**y of soraf**E**nib in lo**C**ally advanced or metastat**I**c patient**S** with radioactive **I**odine refractory thyr**O**id ca**Nc**er) trial, an international, multicenter, placebo-controlled study.

"The DECISION trial results show sorafenib's ability to extend progression-free survival compared to placebo in patients with this type of advanced thyroid cancer," said Marcia Brose, MD, PhD, assistant professor in the Department of Otorhinolarlyngology: Head and Neck Surgery and the division of Hematology/Oncology in the Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania. "Physicians now have an approved treatment option that may help improve care in this patient population."

A total of 417 patients with locally recurrent or metastatic, progressive differentiated thyroid carcinoma refractory to radioactive iodine treatment were randomized to receive 400 mg of oral sorafenib twice daily (207 patients) or matching placebo (210 patients). Metastases were present in 96% of the patients: lungs in 86%, lymph nodes in 51%, and bone in 27%.

Sorafenib significantly extended progression-free survival (PFS), the primary endpoint of the study. The median PFS was 10.8 months (95% CI 9.1-12.9) among patients treated with sorafenib compared to 5.8 months (95% CI 5.3-7.8) among patients receiving placebo (HR=0.59 [95% CI, 0.46, 0.76]; p<0.001). PFS was evaluated by an independent radiological review committee using modified Response Evaluation Criteria in Solid Tumors (mRECIST).

Safety and tolerability were also evaluated. The most common adverse reactions reported for NEXAVAR-treated patients vs. placebo-treated patients in DTC, respectively, were: Palmar-plantar erythrodysesthesia syndrome (PPES) (69% vs. 8%), diarrhea (68% vs. 15%), alopecia (67% vs. 8%), weight loss (49% vs. 14%), fatigue (41% vs. 20%), hypertension (41% vs. 12%), rash (35% vs. 7%), decreased appetite (30% vs. 5%), stomatitis (24% vs. 3%), nausea (21% vs. 12%), pruritus (20% vs. 11%), and abdominal pain (20% vs. 7%). Grade 3/4 adverse reactions were 65% vs. 30%. Drug-related adverse reactions that resulted in treatment discontinuation were reported in 14% of NEXAVAR-treated patients compared to 1.4% of placebo-treated patients.

About Thyroid Cancer

Thyroid cancer has become one of the fastest-increasing cancers in recent years and is the sixth most common cancer in women.[1,2] There are more than 213,000 new cases of thyroid cancer annually and approximately 35,000 people die from thyroid cancer worldwide each year.[3]

Papillary, follicular and Hurthle cell types of thyroid cancer are classified as "differentiated thyroid cancer" and account for approximately 94 percent of all thyroid cancers.[4] While the majority of differentiated thyroid cancers are treatable, locally recurrent or metastatic, progressive, differentiated thyroid carcinoma refractory to radioactive iodine treatment is more difficult to treat.[4,5]

About NEXAVAR® (sorafenib) Tablets

NEXAVAR is approved in the U.S. for the treatment of patients with unresectable hepatocellular carcinoma, patients with advanced renal cell carcinoma and patients with locally recurrent or metastatic, progressive, differentiated thyroid carcinoma refractory to radioactive iodine treatment. NEXAVAR is thought to inhibit both the tumor cell and tumor vasculature. In in vitro studies, NEXAVAR has been shown to inhibit multiple kinases thought to be involved in both cell proliferation (growth) and angiogenesis (blood supply) – two important processes that enable cancer growth. These kinases include Raf kinase, VEGFR-1, VEGFR-2, VEGFR-3, PDGFR-B, KIT, FLT-3 and RET.

NEXAVAR is currently approved in more than 100 countries. NEXAVAR is also being evaluated by Bayer and Onyx, international study groups, government agencies and individual investigators in a range of cancers.

NEXAVAR is co-developed by Onyx and Bayer, except in Japan where Bayer manages all development. The companies co-promote NEXAVAR in the U.S. Outside of the U.S. Bayer has exclusive marketing rights, and Bayer and Onyx share profits globally, excluding Japan.

Onyx and Bayer offer a patient assistance program REACH (Resources for Expert Assistance and Care Helpline) for patients who are not able to pay for NEXAVAR. The companies also provide financial support to co-pay foundations. For more information, visit www.NEXAVAR-us.com.

Important Safety Considerations For NEXAVAR® (sorafenib) Tablets
NEXAVAR in combination with carboplatin and paclitaxel is contraindicated in patients with squamous cell lung cancer.

Cardiac ischemia and/or myocardial infarction may occur. The incidence of cardiac ischemia/infarction in NEXAVAR-treated vs. placebo-treated patients was 2.7% vs. 1.3%, 2.9% vs. 0.4%, and 1.9% vs. 0% in the HCC, RCC, and DTC studies, respectively. Temporary or permanent discontinuation of NEXAVAR should be considered in patients who develop cardiac ischemia and/or myocardial infarction.

An increased risk of bleeding may occur following NEXAVAR administration. The following bleeding adverse reactions were reported in the NEXAVAR-treated vs. placebo-treated patients, respectively, in the HCC study: bleeding from esophageal varices (2.4% vs. 4%) and bleeding with fatal outcome at any site (2.4% vs. 4%); in the RCC study: bleeding regardless of causality (15.3% vs. 8.2%), Grade 3 bleeding (2.0% vs. 1.3%), Grade 4 bleeding (0% vs. 0.2%), and one fatal hemorrhage in each treatment group; in the DTC study: bleeding (17.4% vs. 9.6%) and Grade 3 bleeding (1% vs. 1.4%). If bleeding necessitates medical intervention, consider permanent discontinuation of NEXAVAR.

Hypertension may occur early in the course of treatment. Monitor blood pressure weekly during the first 6 weeks and periodically thereafter, and treat, if required.

Hand-foot skin reaction and rash are common and management may include topical therapies for symptomatic relief. In cases of any severe or persistent adverse reactions, temporary treatment interruption, dose modification, or permanent discontinuation of NEXAVAR should be considered. NEXAVAR should be discontinued if Stevens-Johnson syndrome or toxic epidermal necrolysis are suspected as these may be life-threatening.

Gastrointestinal perforation was an uncommon adverse reaction and has been reported in less than 1% of patients taking NEXAVAR. Discontinue NEXAVAR in the event of a gastrointestinal perforation.

Patients taking concomitant warfarin should be monitored regularly for changes in prothrombin time (PT), International Normalized Ratio (INR), or clinical bleeding episodes.

Temporary interruption of NEXAVAR therapy is recommended in patients undergoing major surgical procedures.

NEXAVAR, in combination with gemcitabine/cisplatin, is not recommended in patients with squamous cell lung cancer. The safety and effectiveness of NEXAVAR has not been established in patients with non-small cell lung cancer.

NEXAVAR can prolong the QT/QTc interval and increase the risk for ventricular arrhythmias. Avoid use in patients with congenital long QT syndrome and monitor patients with congestive heart failure, bradyarrhythmias, drugs known to prolong the QT interval, and electrolyte abnormalities. Interrupt NEXAVAR if QTc interval is greater than 500 milliseconds or for an increase from baseline of 60 milliseconds or greater.

Drug-induced hepatitis with NEXAVAR may result in hepatic failure and death. Liver function tests should be monitored regularly and in cases of increased transaminases without alternative explanation NEXAVAR should be discontinued.

NEXAVAR may cause fetal harm when administered to a pregnant woman. Women of child-bearing potential should be advised to avoid becoming pregnant while on NEXAVAR and female patients should also be advised against breastfeeding while receiving NEXAVAR.

In DTC, NEXAVAR impairs exogenous thyroid suppression. Elevation of thyroid stimulating hormone (TSH) level above 0.5 mU/L was observed in 41% of NEXAVAR-treated patients as compared with 16% of placebo-treated patients in the DTC study. Monitor TSH levels monthly and adjust thyroid replacement medication as needed in patients with DTC.

Elevations in serum lipase and reductions in serum phosphate of unknown etiology have been associated with NEXAVAR.

Avoid concomitant use of strong CYP3A4 inducers, when possible, because inducers can decrease the systemic exposure of sorafenib. NEXAVAR exposure decreases when co-administered with oral neomycin. Effects of other antibiotics on NEXAVAR pharmacokinetics have not been studied.

Most common adverse reactions reported for NEXAVAR-treated patients vs. placebo-treated patients in unresectable HCC, respectively, were: diarrhea (55% vs. 25%), fatigue (46% vs. 45%), abdominal pain (31% vs. 26%), weight loss (30% vs. 10%), anorexia (29% vs. 18%), nausea (24% vs. 20%), and hand-foot skin reaction (21% vs. 3%). Grade 3/4 adverse reactions were 45% vs. 32%.

Most common adverse reactions reported for NEXAVAR-treated patients vs. placebo-treated patients in advanced RCC, respectively, were: diarrhea (43% vs. 13%), rash/desquamation (40% vs. 16%), fatigue (37% vs. 28%), hand-foot skin reaction (30% vs. 7%), alopecia (27% vs. 3%), and nausea (23% vs. 19%). Grade 3/4 adverse reactions were 38% vs. 28%.

Most common adverse reactions reported for NEXAVAR-treated patients vs. placebo-treated patients in DTC, respectively, were: Palmar-plantar erythrodysesthesia syndrome (PPES) (69% vs. 8%), diarrhea (68% vs. 15%), alopecia (67% vs. 8%), weight loss (49% vs. 14%), fatigue (41% vs. 20%), hypertension (41% vs. 12%), rash (35% vs. 7%), decreased appetite (30% vs. 5%), stomatitis (24% vs. 3%), nausea (21% vs. 12%), pruritus (20% vs. 11%), and abdominal pain (20% vs. 7%). Grade 3/4 adverse reactions were 65% vs. 30%.

For information about NEXAVAR including U.S. NEXAVAR prescribing information, visit www.NEXAVAR-us.com or call 1.866.NEXAVAR (1.866.639.2827).

About Bayer HealthCare Pharmaceuticals Inc.
Bayer HealthCare Pharmaceuticals Inc. is the U.S.-based pharmaceuticals business of Bayer HealthCare LLC, a subsidiary of Bayer AG. Bayer HealthCare is one of the world's leading, innovative companies in the healthcare and medical products industry, and combines the activities of the Animal Health, Consumer Care, Medical Care, and Pharmaceuticals divisions. As a specialty pharmaceutical company, Bayer HealthCare provides products for General Medicine, Hematology, Neurology, Oncology and Women's Healthcare. The company's aim is to discover and manufacture

products that will improve human health worldwide by diagnosing, preventing and treating diseases.

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.

Forward Looking Statements
Bayer Forward Looking Statements
This news release may contain forward-looking statements based on current assumptions and forecasts made by Bayer Group or subgroup management. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in Bayer's public reports which are available on the Bayer Web site at www.bayer.com. The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.

Amgen Forward Looking Statements
This news release contains forward-looking statements that are based on management's current expectations and beliefs 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, including Amgen'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's most recent Forms 10-K, 10-Q and 8-K for additional information on the uncertainties and risk factors related to our business. Unless otherwise noted, Amgen is providing this information as of Oct. 4, 2013, 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 we project. 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 us to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and we expect similar variability in the future. We develop 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 we may have believed at the time of entering into such relationship. Also, we or others could identify safety, side effects or manufacturing problems with our products after they are on the market. Our business may be impacted by government investigations, litigation and product liability claims. If we fail to meet the compliance obligations in the corporate integrity agreement between us and the U.S. government, we could become subject to significant sanctions. We depend on third parties for a significant portion of our manufacturing capacity for the supply of certain of our current and future products and limits on supply may constrain sales of certain of our current products and product candidate development.

In addition, sales of our products 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 our products. In addition, we compete with other companies with respect to some of our marketed products as well as for the discovery and development of new products. We believe that some of our newer products, product candidates or new indications for existing products, may face competition when and as they are approved and marketed. Our products may compete against products that have lower prices, established reimbursement, superior performance, are easier to administer, or that are otherwise competitive with our products. In addition, while we routinely obtain patents for our products and technology, the protection offered by our patents and patent applications may be challenged, invalidated or circumvented by our competitors and there can be no guarantee of our ability to obtain or maintain patent protection for our products or product candidates. We cannot guarantee that we will be able to produce commercially successful products or maintain the commercial success of our existing products. Our stock price may be affected by actual or perceived market opportunity, competitive position, and success or failure of our products or product candidates. Further, the discovery of significant problems with a product similar to one of our products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on our business and results of operations.

NEXAVAR® is a registered trademark of Bayer AG.

*Editor's note: Dr. Brose has received consulting fees and honoraria from Bayer HealthCare and Onyx Pharmaceuticals.

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