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Investor News

Bayer and Onyx Announce New Data on Dual Mechanism of Action of BAY 43-9006

Updated Phase II Data Evaluating Novel Signal Transduction Inhibitor in Kidney Cancer Also Released

WEST HAVEN, CT and RICHMOND, CA – Bayer Pharmaceuticals Corporation (NYSE: BAY) and Onyx Pharmaceuticals, Inc. (Nasdaq: ONXX) announced today new preclinical data on the proposed anti-tumor activity of the investigational drug BAY 43-9006, indicating that the novel signal transduction inhibitor exhibits a dual mechanism of action targeting both cell proliferation and angiogenesis (the formation of new blood vessels to support cancer cell growth). The data were presented at the American Association for Cancer Research-National Cancer Institute-European Organization for Research and Treatment of Cancer (AACR-NCI-EORTC) meeting in Boston, USA.

BAY 43-9006 is the first compound that is known to target both Raf kinase and VEGFR2 to inhibit two essential mechanisms involved in tumor growth. Raf kinase is a key enzyme in an important growth signaling pathway associated with the proliferation of tumor cells. VEGFR2 is a main receptor of the vascular endothelial growth factor (VEGF), which plays a key role in angiogenesis.

Additionally, updated Phase II clinical data was presented at the meeting, evaluating BAY 43-9006 as a potential treatment of advanced renal cell carcinoma (RCC, or kidney cancer).

“BAY 43-9006 exhibits dual activity in important mechanisms that inhibit cancer progression. These findings suggest that BAY 43-9006 may have a potential role in the treatment of a range of cancers," said Susan Kelley, M.D., vice president, Oncology, Bayer Pharmaceuticals Corporation. “Besides kidney cancer, Bayer and

Onyx are also evaluating this novel compound as a treatment for melanoma, liver, pancreatic and other cancers."

Interim Phase II Study Results

Bayer and Onyx also released an updated data analysis of Phase II clinical results that were first presented in October 2003. The updated data analysis included 50 participants with advanced and progressive RCC who were evaluable after 12 weeks of treatment. Of the evaluable patients, 42 percent (21 patients) had tumor shrinkage of at least 25 percent at the week 12 assessment. Twenty-six percent (13 patients) had their tumors stabilized within 25 percent of pretreatment size. Overall, 68 percent (34 patients) of this cohort of study participants did not demonstrate tumor progression by the 12-week evaluation point, as assessed by the physicians conducting the clinical trial. The remaining 32 percent (16 patients) discontinued study treatment either because of progressive disease or adverse effects. These early data are subject to confirmation and to a final independent review at the conclusion of the study, at which time the final results will be released.

The five-center, Phase II randomized discontinuation study incorporates a study design that consists of two phases: a 12-week induction phase followed by a randomization phase. During the induction phase, all study participants received BAY 43-9006 orally at 400mg twice a day, administered as a single agent.

"BAY 43-9006 continues to demonstrate potential as a treatment for patients with progressive renal cell carcinoma, with a frequency of tumor shrinkage and disease stabilization rates that remain encouraging as we analyze additional patient experience from this clinical trial," said Mark J. Ratain, M.D., the Phase II study's lead investigator and professor of medicine and associate director for Clinical Sciences, Cancer Research Center, University of Chicago, USA.

All patients with RCC who participated in the trial had progressive disease on study entry. In the study, the most commonly reported drug-related events include: mild-to-moderate hand-foot syndrome, rash, diarrhea, and hypertension, which were shown to be manageable and reversible.

The participants in this study with RCC are part of a larger study population, which totals 342 participants, with advanced refractory solid tumors of multiple types, including RCC (73), melanoma (31), colorectal (115) and others (123) including pancreas, ovarian and breast carcinoma.

Based on the results observed in kidney cancer, Bayer and Onyx have begun an international, multi-center Phase III trial to further evaluate the safety and efficacy of BAY 43-9006. More than 800 people with advanced renal cell carcinoma will participate in the Phase III study at sites worldwide. The primary objective of this randomized study is to confirm the early suggestions of clinical activity of BAY 43-9006 in RCC, using improvement in survival as the primary endpoint for assessment of clinical benefit. The study also will assess time-to-tumor progression, overall response rate, quality of life and the pharmacokinetics of BAY 43-9006.

In other clinical studies, BAY 43-9006 is being evaluated in a Phase II study in participants who have advanced hepatocellular carcinoma (liver cancer), as well as in eight ongoing Phase Ib studies where BAY 43-9006 is combined with standard cytotoxic chemotherapeutic agents. In preliminary findings reported to date, preliminary anti-cancer activity has been observed across a number of tumor types.

BAY 43-9006 Mechanism of Action
BAY 43-9006, an investigational novel signal transduction inhibitor, is the first compound to target both the Raf/MEK/ERK pathway to inhibit tumor cell proliferation and the VEGFR-2 signaling cascade to inhibit tumor angiogenesis.

The Raf/MEK/ERK signalling pathway is an important mediator of responses to growth factors. Activation of growth factor receptors leads to subsequent activation of the MAP kinase pathway downstream of Raf kinase, leading to cell proliferation. Inhibition of the MAP kinase pathway through inhibition of Raf kinase most likely results in anti-proliferative effects with slowing or inhibition of tumor cell proliferation.

In endothelial cells, BAY 43-9006 exerts an anti-proliferative effect by blocking the VEGFR-2 pathway at two levels: upstream by inhibiting the VEGFR-2 receptor and downstream at the level of Raf kinase. It is believed that these activities lead to anti-angiogenesis activity.

"With its dual mechanism of action, BAY 43-9006 may provide an important new approach for treating kidney cancer, a treatment area where there is significant unmet medical need," said Dr Scott Wilhelm, associate director Oncology, Bayer Pharmaceuticals Corporation.

About Kidney Cancer

Renal cell carcinoma is the most common form of kidney cancer. Despite advances in understanding the growth mechanisms of many different tumor types, kidney cancer is still not fully understood. It is believed that both the Ras signaling pathway and angiogenesis may play a role in kidney cancer.

Currently, median survival for patients with advanced metastatic kidney cancer is estimated at eight to 12 months, with five-year survival of less than 10 percent.[1,2] Approximately 190,000 people worldwide are diagnosed with kidney cancer each year, and over 91,000 die from the disease annually.[3]

The primary therapy for localized kidney cancer is surgery.[4] Advanced kidney cancer is generally resistant to chemotherapy treatment, with reported response rates (50 percent shrinkage) of less than 10 percent.[2,5] Immune modulators, such as interferon-alpha and interleukin-2 (IL-2), are currently used as systemic treatment for some patients with advanced disease, but response rates remain low, at about 15 percent. Occasionally, a few patients undergoing systemic therapy do experience long-lasting remission.[6,7,8,9] However, the toxicity of high-dose IL-2, the only treatment approved for the treatment of advanced kidney cancer, limits its use.[10,11]

About Bayer and Onyx Co-development Collaboration

BAY 43-9006 is being co-developed by Bayer and Onyx. The co-development collaboration results in Onyx funding 50 percent of the development and marketing costs for BAY 43-9006. In return, Onyx has a 50/50 profit share in the United States, where the companies can co-promote the product. Everywhere else in the world except Japan, Onyx's share is less than 50 percent, since Bayer has exclusive marketing rights. In Japan, Bayer will fund product development, and Onyx will receive a royalty.

About Onyx Pharmaceuticals

Onyx Pharmaceuticals is engaged in the development of novel cancer therapies that target the molecular basis of cancer. With its partners, the company is developing small molecule drugs. One of these drugs, BAY 43-9006, is in co-development with Bayer Pharmaceuticals Corporation. For more information about Onyx's pipeline and activities, visit the company's website at www.onyx-pharm.com.

About Bayer Pharmaceuticals Corporation

Bayer Pharmaceuticals Corporation is part of the worldwide operations of Bayer HealthCare, a subgroup of Bayer AG. Bayer HealthCare is one of the world's leading innovators in the health care and medical products industry.

Bayer HealthCare combines the global activities of the business groups of Bayer AG in the fields of Biological Products, Consumer Care, Diagnostics, Animal Health and Pharmaceuticals. More than 34,000 employees support the worldwide operations of Bayer HealthCare.

Our work at Bayer HealthCare is to discover, manufacture and market innovative products for the purpose of improving human and animal health worldwide. Our products enhance well being and quality of life by diagnosing, preventing and treating disease.

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Forward-looking statements

This news release contains forward-looking statements based on current assumptions and forecasts made by Bayer Group 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 our public reports filed with the Frankfurt Stock Exchange and with the U.S. Securities and Exchange Commission (including our Form 20-F). The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.