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Investor News

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Bayer's Stivarga® (regorafenib) Tablets Approved by U.S. FDA for Treatment of Patients with Gastrointestinal Stromal Tumors

Stivarga shown in a pivotal Phase III trial to significantly improve progression-free survival in patients with gastrointestinal stromal tumors (GIST) whose disease had progressed after previous treatments

Leverkusen, Germany, February 25, 2013 – Bayer HealthCare announced today that the U.S. Food and Drug Administration (FDA) approved Bayer's Stivarga® (regorafenib) tablets to treat patients with locally advanced, unresectable or metastatic gastrointestinal stromal tumor (GIST) who have been previously treated with imatinib mesylate and sunitinib malate. The approval of Stivarga in GIST is based on results from the pivotal Phase III study (GRID) that demonstrated a statistically significant improvement in progression-free survival (PFS) compared to placebo in patients with GIST whose disease had progressed after treatment with imatinib mesylate and sunitinib malate.

Stivarga is already approved by the FDA for the treatment of patients with metastatic colorectal cancer (mCRC) who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF therapy, and, if KRAS wild type, an anti-EGFR therapy. Stivarga is an oral multi-kinase inhibitor that targets oncogenesis, tumor angiogenesis and maintenance of the tumor microenvironment.

"The second approval for Bayer's Stivarga in the U.S. reveals the drug's potential to fulfill serious unmet medical needs for patients with cancer who require new medicines that continue to slow the progression of their disease," said Kemal Malik, MD, member of the Bayer HealthCare Executive Committee and Head of Global Development. "We look forward to being able to offer benefit to patients with this rare but aggressive disease who have no other approved treatment options, and we will continue to make investments that will bring innovative therapies to patients."

“While great progress has been made in the treatment of GIST since the introduction of kinase inhibitors as effective therapies for this orphan disease, we have been looking for additional, effective treatments for GIST patients whose disease worsens despite currently approved therapies,” said George D. Demetri, MD, Principal Investigator of the GRID study and Director of the Center for Sarcoma and Bone Oncology at the Dana-Farber Cancer Institute in Boston, MA (USA). “These data show that regorafenib can slow disease progression in patients who are no longer responding to other approved therapies and may provide another avenue for GIST patients who would otherwise have no FDA-approved treatment option.”

The pivotal Phase III GRID (GIST – Regorafenib In Progressive Disease) trial showed that regorafenib plus best supportive care (BSC) statistically significantly improved PFS compared to placebo plus BSC (HR=0.27 [95% CI 0.19-0.39], p<0.0001) in patients with metastatic or unresectable GIST who have been previously treated with imatinib mesylate and sunitinib malate. The median PFS was 4.8 months in the regorafenib arm versus 0.9 months in the placebo arm (p<0.0001). There was no statistically significant difference in overall survival at the time of the planned interim analysis based on 29% of the total events for the final analysis. At the time of disease progression as assessed by central review, the study blind was broken and all patients were offered the opportunity to take regorafenib at the investigator’s discretion. 56 (85%) patients randomized to placebo and 41 (31%) patients randomized to regorafenib received open-label regorafenib.

In clinical trials, the most frequently reported drug-related adverse events (≥20%) in regorafenib-treated patients versus placebo-treated patients were asthenia/fatigue, hand-foot skin reaction (HFSR), diarrhea, decreased appetite and food intake, hypertension, mucositis, dysphonia, infection, pain (not otherwise specified), decreased weight, gastrointestinal and abdominal pain, rash, fever and nausea. The most serious adverse drug reactions in patients receiving Stivarga are hepatotoxicity, hemorrhage, and gastrointestinal perforation. The U.S. Stivarga label includes a boxed warning citing the risk of hepatotoxicity.

Results from the GRID study were presented at the Annual Meeting of the American Society of Clinical Oncology (ASCO) in June 2012 and published online on November 22, 2012 in the journal *The Lancet*.

Stivarga was developed under the Fast Track program and received priority review designations for metastatic or unresectable GIST and mCRC from the FDA. These

designations are granted by the FDA to expedite the development and review of drugs to treat serious diseases and fulfill an unmet medical need, and are given to drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists.

About the GRID Study

GRID was a randomized, double-blind, placebo-controlled, multi-center Phase III study of regorafenib for the treatment of GIST. It randomized 199 patients with unresectable, locally advanced or metastatic GIST, who had been previously treated with imatinib mesylate and sunitinib malate.

Patients were randomized in a 2:1 ratio to receive either regorafenib plus BSC or placebo plus BSC to evaluate efficacy and safety. Randomization was stratified by line of therapy (third vs. four or more) and geographic region (Asia vs. rest of the world). Treatment cycles consisted of 160 mg regorafenib (or matching placebo) once daily for three weeks on / one week off plus BSC. The primary endpoint was PFS, and secondary endpoints included OS, time to progression, disease control rate, tumor response rate, and duration of response. The safety and tolerability of the two treatment groups were also compared.

About Gastrointestinal Stromal Tumor (GIST)

GIST is the most common form of sarcoma arising from the muscle wall of the gastrointestinal tract. GIST represents a life-threatening malignancy if the disease has spread to other parts of the body (metastasized) or is unable to be surgically removed with curative intent. The incidence of GIST is estimated to be 11 to 20 patients per million per year.

The discovery of oncogenic KIT kinase mutations in GISTs and the introduction of kinase inhibitor therapies have led to a rapid evolution in the understanding of these tumors. It is now established that 70–80% of GISTs harbour a KIT gene mutation, that these mutations lead to the continued activation of the kinase and that mutant KIT is a clinically important therapeutic target in GIST.

About Stivarga® (regorafenib)

Stivarga® (active substance regorafenib) is an oral multi-kinase inhibitor that targets oncogenesis, tumor angiogenesis and maintenance of the tumor microenvironment signaling by inhibiting multiple protein kinases. In preclinical studies, Stivarga has been shown to inhibit several angiogenic VEGF receptor kinases that play a role in tumor neoangiogenesis (the growth of new blood vessels). It also inhibits various oncogenic and

tumor microenvironment kinases including KIT and PDGFR, which play a key role in the development and recurrence of GIST.

Bayer has also submitted for marketing approval of regorafenib for the treatment of mCRC in the EU in May 2012. The new drug application for regorafenib for the treatment of advanced CRC filed in Japan in July 2012 was granted priority review. In December 2012, Bayer submitted a filing in Japan for regorafenib for the treatment of GIST.

Regorafenib is a Bayer compound developed by Bayer and jointly promoted by Bayer and Onyx Pharmaceuticals, Inc. in the U.S. In 2011, Bayer entered into an agreement with Onyx, under which Onyx receives a royalty on all global net sales of regorafenib in oncology.

About Bayer HealthCare

The Bayer Group is a global enterprise with core competencies in the fields of health care, agriculture and high-tech materials. Bayer HealthCare, a subgroup of Bayer AG with annual sales of EUR 17.2 billion (2011), is one of the world's leading, innovative companies in the healthcare and medical products industry and is based in Leverkusen, Germany. The company combines the global activities of the Animal Health, Consumer Care, Medical Care and Pharmaceuticals divisions. Bayer HealthCare's aim is to discover, develop, manufacture and market products that will improve human and animal health worldwide. Bayer HealthCare has a global workforce of 55,700 employees (Dec 31, 2011) and is represented in more than 100 countries. More information at www.healthcare.bayer.com.

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