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Investor News

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Stivarga® (regorafenib) from Bayer Approved in the European Union for the Treatment of Gastrointestinal Stromal Tumors

- Approval in the second indication for Stivarga in the EU within one year
- Decision based on positive results from Phase III GRID trial in which regorafenib significantly extended progression-free survival

Leverkusen, Germany, July 30, 2014 – The oncology compound Stivarga® (regorafenib) from Bayer has been approved by the European Commission (EC) for the treatment of adult patients with unresectable or metastatic gastrointestinal stromal tumors (GIST) who progressed on or are intolerant to prior treatment with imatinib and sunitinib. 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 prior treatments. Stivarga is already approved in the EU for the treatment of patients with metastatic colorectal cancer (mCRC).

“Following the approval of Stivarga for GIST in several countries worldwide, including the U.S. and Japan, we are delighted to offer patients in Europe a new option for treating this rare yet relentless cancer,” said Dr. Joerg Moeller, Member of the Bayer HealthCare Executive Committee and Head of Global Development. “At Bayer, we are dedicated to exploring solutions for different tumor types and drive innovation to meet the unmet needs of both physicans and patients.”

“GIST is a highly aggressive cancer that can go undetected for years and, at the point of diagnosis, most patients have already progressed to advanced stages of disease. Survival rates are low and treatments are limited after imatinib and sunitinib,” said Jean Yves-Blay, GRID investigator, Professor of Medicine in Medical Oncology and Head of the Medical Oncology Department, Centre Leon Berard at Université Claude Bernard in Lyon, France. “The Phase III GRID trial demonstrated that progression-free survival with

regorafenib is more than five times than with placebo, a significant improvement for those who have progressive disease."

"One of the hardest things to hear from your doctor is that there is no treatment left for your disease," said Markus Wartenberg, Member of the Board of Directors of the Sarcoma Patients EuroNet Association (SPAEN). "In rare cancers such as GIST, hope empowers people to continue fighting the cancer. New treatment options are welcomed so that patients can continue to defy their illness."

The results of the pivotal Phase III GRID study showed that regorafenib plus best supportive care (BSC) significantly improved progression-free survival (PFS) compared to placebo plus BSC (HR=0.268 [95% CI 0.185-0.388], p<0.0001) in patients with metastatic and/or unresectable GIST who were previously treated with imatinib and sunitinib, reducing the risk of progression or death by 73%. The median PFS was 4.8 months in the regorafenib arm versus 0.9 months in the placebo arm (p<0.0001). The increase in PFS was consistent and independent of patient age, sex, geographic region, prior lines of treatment or ECOG performance status.

In clinical trials, the most frequently reported drug-related adverse events in regorafenib-treated patients versus placebo-treated patients, respectively, were: asthenia/fatigue, hand-foot skin reaction (HFSR) / palmar-plantar erythrodysesthesia (PPE), 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 regorafenib are hepatotoxicity, hemorrhage, and gastrointestinal perforation. Adverse events in regorafenib-treated patients generally occur early (within the first two treatment cycles), therefore it is advised to monitor patients closely.

Full results from the GRID study were presented at the 48th Annual Meeting of the American Society of Clinical Oncology (ASCO) in June 2012 and published in November 2012 in *The Lancet*.

Regorafenib has been approved under the brand name Stivarga® in several countries, including the U.S. and Japan, for the treatment of GIST. In 60 countries worldwide, including the U.S., Europe and Japan, the product has also been approved for the treatment of patients with metastatic colorectal cancer (mCRC).

About the GRID Study

GRID (GIST – Regorafenib In Progressive Disease) was a randomized, double-blind, placebo-controlled, multi-center Phase III study of regorafenib for the treatment of GIST. It randomized 199 patients whose disease had progressed despite prior treatment with imatinib and sunitinib.

Patients were randomized in a 2:1 ratio to receive either regorafenib plus BSC or placebo plus BSC to evaluate efficacy and safety. 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. Patients initially randomized to placebo were allowed to cross over to open-label regorafenib once the disease progressed.

About Gastrointestinal Stromal Tumors (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. GIST affects an estimated 11-20 patients per million per year worldwide.

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 harbor 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® (regorafenib) is an oral multi-kinase inhibitor that inhibits various kinases within the mechanisms involved in tumor growth and progression – angiogenesis, oncogenesis and the tumor microenvironment. In preclinical studies, Stivarga inhibits several angiogenic VEGF receptor tyrosine kinases that play a role in tumor neoangiogenesis (the growth of new blood vessels). In addition to VEGFR 1-3 it also inhibits various oncogenic and tumor microenvironment kinases including TIE-2, RAF-1, BRAF, BRAFV600, KIT, RET, PDGFR, and FGFR, which individually and collectively impact upon tumor growth, formation of a stromal microenvironment and disease progression.

Stivarga is a compound developed by Bayer. In 2011, Bayer entered into an agreement with Onyx Pharmaceuticals, Inc., an Amgen subsidiary, under which Onyx receives a royalty on all global net sales of Stivarga in oncology.

About Oncology at Bayer

Bayer is committed to delivering *science for a better life* by advancing a portfolio of innovative treatments. The oncology franchise at Bayer now includes three oncology products and several other compounds in various stages of clinical development. Together, these products reflect the company's approach to research, which prioritizes targets and pathways with the potential to impact the way that cancer is treated.

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 18.9 billion (2013), 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 56,000 employees (Dec 31, 2013) and is represented in more than 100 countries. More information is available at www.healthcare.bayer.com.

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