

## First New Drug Therapy in 30 Years Offers Hope to Liver Cancer Patients

*NEXAVAR the Only Drug Therapy Proven to Significantly Improve Overall Survival*

**Toronto, ON – February 4, 2008** – Bayer Inc. announced today that Health Canada has approved a new indication for NEXAVAR® (sorafenib tablets) for the treatment of patients with unresectable hepatocellular carcinoma (HCC), or liver cancer. NEXAVAR, an oral anti-cancer treatment, is the first approved drug therapy for liver cancer, and the only one shown to significantly improve overall survival in HCC patients who previously were without adequate treatment options.

"The approval of NEXAVAR in Canada for the treatment of HCC represents a major advance for this patient population," said Dr. Morris Sherman, a clinical hepatologist in Toronto and Associate Professor of Medicine. "Liver cancer is a disease that traditionally has poor patient outcomes and until now, there were no approved drug therapies for these patients, making their prognosis extremely grim. NEXAVAR is a simple, non-invasive and effective treatment for HCC, offering patients a greater chance of significantly extending their overall survival."

Health Canada's decision to approve NEXAVAR was based on positive data from the international Phase 3 placebo-controlled **S**orafenib **H**CC **A**ssessment **R**andomized **P**rotocol (SHARP) trial, which demonstrated that NEXAVAR extended overall survival by 44 per cent in patients with HCC (HR=0.69; p=0.0006) versus placebo. In the study, median overall survival was 10.7 months in NEXAVAR-treated patients compared to 7.9 months in those taking placebo. No indication of imbalances was observed in serious adverse events between the NEXAVAR and placebo-treated groups, with the most commonly observed adverse events in patients receiving NEXAVAR being diarrhea and hand-foot skin reaction.

"When I was told I had liver cancer and that it had progressed to a stage where chemotherapy was no longer an option, I was devastated," said Wally Wasylyk of Craven, Saskatchewan. "After 16 months of taking NEXAVAR in a clinical study, my cancer is in remission and I now have a second chance at life."

### **About Liver Cancer**

Hepatocellular carcinoma is the most common form of liver cancer and is responsible for approximately 90 per cent of the primary malignant liver tumours in adults.<sup>1,2</sup> It is the fifth most common cancer in the world<sup>3</sup> and the third leading cause of cancer-related deaths globally.<sup>4</sup> Incidence of and mortality rates for liver cancer in Canada are on the rise, and for 2007, it is estimated that there will be approximately 1,350 newly diagnosed cases of liver cancer, an estimated half of which will be fatal.<sup>5,6</sup> Liver cancer is more prevalent in men than women, with 1,040 new diagnoses in men, compared to 310 in women.<sup>7</sup>

"During the 30 years that HCC has been recognized as a form of cancer, there has never been an approved drug treatment that improves survival for patients suffering from this devastating disease," said Dr. Shurjeel Choudhri, senior vice president, head of Medical and Scientific Affairs, Bayer HealthCare Pharmaceuticals. "This indication for NEXAVAR in Canada, within two years of the drug's original approval for kidney cancer, demonstrates Bayer's commitment to expediting the clinical development of innovative therapies."

## **About NEXAVAR**

NEXAVAR targets both the tumour cell and tumour vasculature and is the only oral multi-kinase inhibitor that does not require liver cancer patients to interrupt their treatment schedule. In preclinical studies, NEXAVAR has been shown to target members of two classes of kinases known to be involved in both cell proliferation (growth) and angiogenesis (growth of new blood vessels) – two important processes that enable cancer growth. NEXAVAR works by slowing tumour growth and by cutting off the blood supply to the tumour (angiogenesis). NEXAVAR acts on proteins called kinases which include RAF kinase, VEGFR-2, VEGFR-3, PDGFR- $\beta$ , KIT, FLT-3 and RET.

NEXAVAR is also currently approved in more than 60 countries, including Canada, the United States and in the European Union, for the treatment of patients with advanced kidney cancer. In 2006, Therapeutic Products Directorate of Health Canada (TPD) granted a Notice of Compliance with Conditions (NOC/c) for NEXAVAR for treatment of patients with locally advanced / metastatic renal cell (clear cell) carcinoma, who have failed prior cytokine therapy or considered unsuitable for such therapy. This authorization reflects the promising nature of the clinical evidence which will require additional confirmatory data. Products approved under Health Canada's NOC/c policy have demonstrated promising benefit, are of high quality and possess an acceptable safety profile based on a benefit/risk assessment for the approved use.

Currently, NEXAVAR is funded for primary liver cancer in British Columbia and Quebec on a patient by patient basis. In Ontario, NEXAVAR has been denied rapid review. It is now under review by the Joint Oncology Drug Review (JODR) managed by Ontario. Bayer has also submitted applications to all other provincial government authorities through the JODR Process.

## **Important Safety Considerations for Canadian Patients Taking NEXAVAR**

Based on the currently approved product monograph for the treatment of patients with HCC and locally advanced/metastatic kidney cancer (renal cell carcinoma or RCC), hypertension may occur early in the course of therapy and blood pressure should be monitored weekly during the first six weeks of therapy and treated as needed. In the pivotal liver cancer study, incidence of bleeding regardless of causality was reported in 18 per cent of NEXAVAR treated patients and 20 per cent of placebo patients. Incidence of cardiac ischemia/infarction was 2.7 per cent for NEXAVAR and 1.3 per cent for placebo. CTCAE Grade 3 adverse events were reported in 39 per cent of patients receiving NEXAVAR compared to 24% of patients receiving placebo. CTCAE Grade 4 adverse events were reported in 6 per cent of patients receiving NEXAVAR compared to 8 per cent of patients receiving placebo. Overall, the most common adverse events ( $\geq 20$  per cent) which were considered to be related to NEXAVAR in patients with HCC or RCC are fatigue, weight loss, rash/desquamation, hand-foot skin reaction, alopecia, diarrhea, anorexia, nausea, and abdominal pain.

In the kidney cancer studies, incidence of bleeding regardless of causality was 15 per cent for NEXAVAR versus 8 per cent for placebo and the incidence of treatment-emergent cardiac ischemia/infarction was 2.9 per cent for NEXAVAR versus 0.4 per cent for placebo. Most common treatment-emergent adverse events with NEXAVAR were diarrhea, rash/desquamation, fatigue, hand-foot skin reaction, alopecia, and nausea. Grade 3/4 adverse events were 38 per cent for NEXAVAR versus 28 per cent for placebo.

Women of child-bearing potential should be advised to avoid becoming pregnant and women with infants should be advised against breast-feeding. In cases of any severe or persistent side effects, temporary treatment interruption, dose modification or permanent discontinuation should be considered.

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NEXAVAR has not been studied in patients who have severe kidney problems (in addition to kidney cancer) or severe liver problems. Of note, possible serious side-effects with NEXAVAR include high blood pressure, bleeding, heart attack and gastrointestinal (bowel) perforation. For Canadian NEXAVAR prescribing information, visit [www.bayerhealth.com](http://www.bayerhealth.com) or call 1-800-265-7382.

### **About Bayer Inc.**

Bayer Inc. (Bayer) is a Canadian subsidiary of Bayer AG, an international research-based group with core businesses in health care, crop science, and innovative materials. Headquartered in Toronto, Ontario, Bayer Inc. operates the Bayer Group's HealthCare and MaterialScience businesses in Canada. Bayer CropScience Inc., headquartered in Calgary, Alberta operates as a separate legal entity in Canada. Together, the companies play a vital role in improving the quality of life for Canadians - producing products that fight diseases, protecting crops and animals, and developing high-performance materials for applications in numerous areas of daily life. Canadian Bayer facilities include the Toronto headquarters and offices in Ottawa and Calgary. Bayer Inc. has approximately 1,000 employees across Canada and had sales of over \$910 million CDN in 2006. Globally, the Bayer Group had sales of over 28 billion Euro in 2006. Bayer Inc. invested approximately \$47 million CDN in research and development in 2006. Worldwide, the Bayer Group spends the equivalent of over 2 billion Euro in 2006 in R&D.

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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 annual and interim reports filed with the Frankfurt Stock Exchange. The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.*

### **References:**

<sup>1</sup> World Health Organization/Hepatitis B. Web site. <http://www.who.int/csr/disease/hepatitis/whocdscsrlyo20022/en/>. Accessed January 15, 2008.

<sup>2</sup> Penn State Milton S. Hershey Medical Center College of Medicine/Malignant Hepatoma. Web site. <http://www.hmc.psu.edu/healthinfo/m/malignantheptoma.htm>. Accessed January 15, 2008.

<sup>3</sup> World Health Organization. Estimates by WHO Region: Incidence. Web site. <http://www.who.int/healthinfo/statistics/gbdwhoregionincidence2002.xls>. Accessed January 15, 2008.

<sup>4</sup> World Health Organization/Cancer Fact Sheet Number 297. Web site. <http://www.who.int/mediacentre/factsheets/fs297/en/print.html>. Accessed January 15, 2008.

<sup>5</sup> Canadian Cancer Society. Canadian Cancer Encyclopedia. Available at: <http://info.cancer.ca/E/CCE/cceexplorer.asp?tocid=25>. Accessed January 9, 2008.

<sup>6</sup> Canadian Cancer Society. Canadian Cancer Encyclopedia. Available at: <http://info.cancer.ca/E/CCE/cceexplorer.asp?tocid=25>. Accessed January 9, 2008.

<sup>7</sup> Canadian Cancer Society. Canadian Cancer Encyclopedia. Available at: <http://info.cancer.ca/E/CCE/cceexplorer.asp?tocid=25>. Accessed January 9, 2008.