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Investor News

# Bayer Initiates Phase III Clinical Study of Trasylol® Therapy During Primary Total Hip Replacement Surgery

Study Examines the Effects of Trasylol in Reducing Blood Loss and the Need for Transfusion

**Leverkusen, April 11, 2005** – Bayer Pharmaceuticals Corporation (NYSE: BAY) today announced the initiation of a Phase III controlled clinical study to evaluate the safety and efficacy of Trasylol® (aprotinin injection) in reducing blood loss and the need for transfusion in patients undergoing elective primary total hip replacement surgery. More than 300,000 hip replacements are performed in the United States each year,[1] and the procedure is associated with significant blood loss.[2]

Trasylol is currently approved for use in more than 60 countries. In the United States, Trasylol is indicated for prophylactic use to reduce perioperative blood loss and the need for blood transfusion in patients undergoing cardiopulmonary bypass (CPB) in the course of coronary artery bypass graft (CABG) surgery. The drug acts by inhibiting multiple mediators resulting in the attenuation of inflammatory responses, which in CABG surgery translates into reduced bleeding and a decreased need for allogeneic (blood donated from another individual) blood transfusions. The double-blind, placebo-controlled trial has been initiated to assess the drug's hemostatic (blood sparing) effects in primary total hip replacement surgery. Patients undergoing primary total hip replacement surgery lose an average of three units of blood, which often must be replaced by a transfusion.[3]

"Current blood supply shortages and the rising cost of this precious commodity, along with potential health risks associated with transfusions, underscore the need for a therapeutic option in this setting," said Dr. David Nazarian, hip and knee replacement specialist at Pennsylvania Hospital in Philadelphia. "Since Trasylol is widely used as

a hemostatic agent in reducing the need for transfusion in CABG surgery, we are investigating its effects in primary total hip replacement where blood loss may result in unnecessary exposure to donor blood."

In the study, 360 patients will be randomly assigned to prophylactically receive 200 mL of intravenous Trasylol or placebo at the start of the operation, followed by 50 mL/hr of either until the surgery is complete. The study is designed to evaluate the effect of Trasylol on the need for transfusion, blood loss, dryness of the surgical field and markers of inflammation. Approximately 34 investigational centers in North America will participate in the study.

"We are encouraged by previous study findings on the blood sparing effects of Trasylol in this setting," said Dr. Paul MacCarthy, Vice President of Medical Affairs at Bayer. "We are hopeful that this clinical trial will validate those findings in this specific patient population."

**Previous Study Results**

Previous prospective, randomized studies evaluating aprotinin therapy in primary hip surgeries demonstrated that the drug significantly decreased perioperative blood loss, red blood cell transfusion and the number of patients exposed to transfusion.[4,5] One study found that the use of high-dose aprotinin during total hip replacement resulted in a reduction in both blood loss and the amount of blood transfused.[4]

In total, more than 1,100 patients undergoing hip replacement surgery have been included in previous Bayer sponsored and independently published studies with Trasylol. In these trials, the incidence of adverse events was comparable to placebo, including the occurrence of deep vein thrombosis. For additional safety information associated with the use of Trasylol, see Important Safety Considerations below.

**About Total Hip Replacement Surgery**

Total hip replacement is a surgical procedure to replace the hip joint, and is usually performed for severe arthritic conditions. During the procedure, the acetabulum (cup-shaped bone in the pelvis) and the femur (thigh bone) are removed and replaced with new artificial parts, typically made from high-density plastic and strong stainless metal or ceramic.[6] Because this surgery involves the removal and replacement of joints, a patient loses a significant amount blood, and a transfusion may be required.[2]

The primary goals of hip replacement surgery are to improve mobility by relieving pain and regenerating overall function of the hip joint.[7] A total hip replacement provides complete or nearly complete pain relief in 90 to 95 percent of patients who undergo the procedure.[6]

Patients usually spend approximately 3 to 5 days in the hospital following the operation.[8] Full recovery from the surgery takes about 3 to 6 months, depending on the overall health of the patient, type of surgery and the success of rehabilitation.[7]

**About Trasylol**

Trasylol, a broad-spectrum proteinase inhibitor, modulates the systemic inflammatory response associated with cardiopulmonary bypass (CPB) in the course of CABG surgery.

Approved by the FDA in 1993, Trasylol is the only product indicated for prophylactic use to reduce perioperative blood loss and the need for blood transfusion in patients undergoing CPB in the course of CABG surgery. Full prescribing and warning information is also available at www.Trasylol.com.[9]

The effects of Trasylol use in CPB involves a reduction of inflammatory response to surgery, reduced bleeding and decreased re-exploration for bleeding, which translates into a decreased need for allogeneic (blood donated from another individual) blood transfusions.

An important part of Bayer Pharmaceuticals Corporation's Specialty Pharmaceuticals portfolio, Trasylol has remained a category leader for several years. Bayer is committed to further investment in the Trasylol franchise and is actively engaged in the research and development of a recombinant version of the product. In anticipation of emerging needs of this market, Bayer is also leading in next generation product development.

**Important Safety Considerations**

Anaphylactic or anaphylactoid reactions are possible when Trasylol is administered. Hypersensitivity reactions are rare in patients with no prior exposure to aprotinin. The risk of anaphylaxis is increased in patients who are reexposed to aprotinin-containing products. The benefit of Trasylol to patients undergoing primary CABG surgery should be weighed against the risk of anaphylaxis should a second exposure to

aprotinin be required (see WARNINGS and PRECAUTIONS in the Trasylol prescribing information).

In clinical studies, hypersensitivity and anaphylactic reactions were:

- rare (<0.1%) in patients with no prior exposure to Trasylol
- 2.7% overall reaction rate upon re-exposure
  - within 6 months, the incidence was 5 percent
  - after 6 months, the incidence was 0.9 percent[9]

Trasylol is generally well tolerated. In clinical trials, graft patency, myocardial infarction, renal or hepatic dysfunction and mortality were comparable to placebo.

**About Bayer Pharmaceuticals Corporation**

Bayer Pharmaceuticals Corporation (www.bayerpharma.com) is part of the worldwide operations of Bayer HealthCare AG, a subsidiary of Bayer AG.

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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.

1. "Arthroplasty and Total Joint Replacement Procedures: 1991 to 2000." Retrieved March 21, 2005, from http://www.aaos.org/wordhtml/research/stats/arthropl.htm#intra07.
2. Tenholder M., Cushner F. "Intraoperative Blood Management in Joint Replacement Surgery." *Orthopedics* 2004: June Supplement. Retrieved March 16, 2005, from http://www.orthobluejournal.com/supp/0604/toc.asp.
3. Toy PT., Kaplan EB., McVay, PA., et al. "Blood loss and replacement in total hip arthroplasty: a multicenter study. The preoperative Autologous Blood Donation Study Group." *Transfusion* 32(1): 63-67, 1992.
4. Murkin JM. "Aprotinin decreases exposure to allogeneic blood during primary unilateral total hip replacement." *J Bone Joint Surg Am* 82(5): 675-684, 2000.
5. Janssens M., Joris J. et al. "High-Dose Aprotinin Reduces Blood Loss in Patients Undergoing Total Hip Replacement Surgery." *Anesthesiology* 80: 23-29, 1994.
6. Total Hip Replacement: A Guide for Patients. Retrieved March 11, 2005, from http://www.vh.org/adult/patient/orthopaedics/hipreplace/#2.
7. Questions and Answers About Hip Replacement. Retrieved March 11, 2005, from http://www.niams.nih.gov/hi/topics/hip/hiprepqa.htm.
8. Solucient, National In-Patient Hospital Database, 2003.
9. Trasylol Prescribing Information. Retrieved August 20, 2004 from http://www.trasylol.com.