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Lilly Plans New Clinical Trial of Xigris(R)

Trial will help better identify appropriate patient, define the benefit-risk profile in this population

INDIANAPOLIS, Feb 26, 2007 /PRNewswire-FirstCall via COMTEX News Network/ -- Eli Lilly and Company (NYSE: LLY) today announced plans for a new clinical study of Xigris(R) (drotrecogin alfa [activated]). The trial is designed to help clinicians better identify severe sepsis patients at high risk of death who are more likely to benefit from this novel therapy and to further clarify the drug's benefit/risk profile. The new trial initiative follows discussions with the European Medicines Agency (EMA) in the context of its fourth annual license reassessment for Xigris.

"Advancements made in sepsis care over the past five years, and ongoing scientific questions surrounding appropriate patient selection for Xigris and about severe sepsis treatment in general make this an opportune time for a new Phase III placebo-controlled study of Xigris," said J. Anthony Ware, M.D., vice president, Lilly Research Laboratories and global platform leader for cardiovascular and acute care. "The trial may provide additional scientific insights and potential patient benefits."

Xigris was licensed in the EU in August 2002 under exceptional circumstances, which establishes an annual review. During each reassessment, the Committee for Medicinal Products for Human Use (CHMP) reviews all existing data. In discussions, Lilly committed to conduct a new placebo-controlled clinical trial to help refine appropriate patient identification for treatment with Xigris. Commercial Xigris will remain available to physicians for treatment of severe sepsis patients within the currently approved label during the course of the trial.

In the United States, where Xigris is licensed for adult patients with severe sepsis (sepsis associated with acute organ dysfunction) at high risk of death, the federal Food and Drug Administration does not annually reassess licensing.

Lilly's medical team is working with medical experts in Europe and the United States to develop a protocol for the international trial involving Xigris, with the primary endpoint being 28-day all-cause mortality. Lilly estimates the trial will begin enrolling patients during the first quarter of 2008 and take approximately two and a half years to complete.

PROWESS(i) - Recombinant Human Activated PROtein C Worldwide Evaluation in Severe Sepsis - the pivotal Phase III registration trial for Xigris, was initiated in July 1998. Enrollment was suspended at the second interim analysis in June 2000 because Xigris demonstrated a significant survival benefit that exceeded the prospectively set stopping rules. The trial showed a relative risk reduction in mortality among high risk patients by 29 percent. Mortality rates were 30.9 percent among drotrecogin alfa (activated)-treated patients vs. 43.7 percent among patients treated with placebo ($p=0.0002$). In patients with multiple organ dysfunction, mortality rates were 26.5 percent among drotrecogin alfa (activated)-treated patients vs. 33.9 percent in patients treated with placebo ($p=0.006$). PROWESS was the first large severe sepsis trial to meet the primary endpoint of a significant reduction in mortality and led to approval of Xigris in more than 50 countries globally.

The new trial will be conducted in patients within the currently indicated population (adults with severe sepsis at high risk of death) and utilize the current standard of care for severe sepsis. It will differ from PROWESS in that it will set further parameters for patient identification and evaluation to identify patients early in the course of sepsis, and to ensure appropriate and adequate patient selection and safety assessments for those receiving the drug.

Xigris is the only approved pharmaceutical therapy specifically indicated in Europe for the treatment of adult patients with severe sepsis with multiple organ failure when added to best standard care. The use of Xigris should be considered mainly in situations when therapy can be started within 24 hours after the onset of organ failure. In the United States Xigris is indicated to reduce mortality in adult patients with severe sepsis (sepsis associated with acute organ dysfunction) at high risk of death.

"Lilly stands firmly behind the PROWESS trial, which led to the approval of Xigris in more than 50 countries," said Mark D. Williams, M.D., medical director for Xigris. "This new study will focus on helping physicians identify the optimal patient for Xigris therapy by further clarifying the benefit-risk profile of this novel therapy."

Several post-marketing studies have provided significant insights into severe sepsis pathophysiology and treatment with Xigris. Lilly is committed to applying this learning in this new clinical trial with these indicated patients -- the adult patient with severe sepsis at high risk of death, Williams said.

In addition to the new placebo-controlled study, a Phase II Xigris clinical trial began in November 2006. RESPOND - Research Evaluating Serial Protein C levels in severe sepsis patients ON Drotrecogin alfa [activated] - is designed to tailor the dose and duration of Xigris based upon serial Protein C levels. Data from this trial could advance Xigris therapy by using a biomarker such as Protein C to provide the right dose of Xigris to the right patient at the right time, said Williams. Five hundred patients are being enrolled at 50 sites in 11 countries for the trial.

About Severe Sepsis

Sepsis is a common, deadly and under-diagnosed disease that claims approximately 1,400 lives worldwide each day. Severe sepsis often develops as a complication after common illnesses such as pneumonia, and bacterial infections. Annually, there are approximately 88 cases of severe sepsis per 100,000 people in Europe and 750,000 cases in the United States, largely as a consequence of rapid organ failure during the most life-threatening stage of the illness -- the first 28 days.(ii)(iii)(iv)

About Xigris

Xigris (drotrecogin alfa [activated]) is a recombinant form of human Activated Protein C. It is administered by intravenous infusion and is available in 5 mg and 20 mg vials. In November 2001, the U.S. Food and Drug Administration approved Xigris for the reduction of mortality in adult patients with severe sepsis (sepsis associated with acute organ dysfunction) who have a high risk of death (e.g., as determined by APACHE II).

Bleeding is the most common serious adverse effect associated with Xigris therapy. In PROWESS, a Phase III study, serious bleeding events were observed during the 28-day study period in 3.5 percent of Xigris-treated and 2.0 percent of placebo-treated patients. The difference in serious bleeding occurred primarily during infusion. Each patient being considered for therapy with Xigris should be carefully evaluated and anticipated benefits weighed against potential risks associated with therapy. For full safety information including contraindications and warnings, please see Xigris Prescribing Information, which can be obtained by visiting <http://www.Xigris.com>.

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of first-in-class and best-in-class pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers -- through medicines and information -- for some of the world's most urgent medical needs. Additional information about Lilly is available at www.lilly.com.

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Xigris(R) (drotrecogin alfa (activated), Lilly)

i The Recombinant Human Activated Protein C Worldwide Evaluation in Severe Sepsis (PROWESS) study was initiated in July 1998. Enrollment was suspended at the second interim analysis in June 2000 because Xigris demonstrated a significant survival benefit that exceeded the prospectively set stopping rules. Analysis indicated a statistically significant 29% relative reduction in risk of death among high-risk (APACHE II score greater than or equal to 25) patients (P=0.0002). In these patients, survival rates were 69% for Xigris patients, compared to 56% for standard therapy patients at 28 days. The difference in survival was sustained through 2.5 years of follow-up.

ii Angus DC et al. Crit Care Med 2001; 29,: 1303-10

iii Davies A et al. A European estimate of the burden of disease in ICU. In preparation.

iv Bone RC et al. Chest 1992; 101:1644-55

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