



## Scios Submits Interim Report to FDA on NATRECOR®(nesiritide) PROACTION Trial

### Scios Submits Interim Report to FDA on NATRECOR®(nesiritide) PROACTION Trial

FREMONT, Calif., Jan 03, 2006 /PRNewswire-FirstCall via COMTEX News Network/ -- Scios Inc. today announced it is submitting an interim report to the U.S. Food & Drug Administration, and other relevant international regulatory authorities, on an ongoing expanded analysis of a three-year-old exploratory health outcomes study (the PROACTION trial) comparing treatment with NATRECOR® (nesiritide) to placebo. The interim report contains two additional deaths that had occurred within 30 days after treatment with NATRECOR® but had not been initially reported to the company.

The two new cases were not included in a report on the PROACTION study that was published in the 2005 October issue of the Journal of Emergency Medicine. In that publication, the difference in all-cause mortality (patient deaths due to all causes, including those unrelated to medical treatment) at 30 days post treatment between the NATRECOR® and placebo arms was not statistically significant. Scios is in the process of finalizing an audit of the 30-day mortality data in conjunction with the expanded analysis. Upon completion, Scios will re-analyze the statistical significance of the 30-day mortality data. In January 2005, Scios agreed with FDA to conduct an expanded analysis of PROACTION to evaluate all-cause mortality through 180 days following treatment with NATRECOR or placebo. This expanded analysis goes beyond the study's original protocol defined 30-day mortality follow-up period. It was in the course of conducting this expanded analysis that the two additional deaths at 30 days post treatment were identified. A final report of this expanded analysis is planned for submission to FDA, as well as to relevant health authorities in other countries, in the first quarter of 2006.

The company is confident these two additional cases have no impact on the overall benefit/risk profile of NATRECOR® when prescribed according to the approved label. The overwhelming body of data generated in large, well- controlled, prospectively designed clinical trials support the efficacy and safety of NATRECOR® as a treatment for patients with acutely decompensated heart failure (ADHF) who have dyspnea (shortness of breath) at rest or with minimal activity (such as talking, eating, bathing). Scios recommends NATRECOR® for use in ADHF patients who present to a hospital setting, such as an emergency room or observation unit, exhibiting these symptoms. Full prescribing information for NATRECOR® is available at <http://www.natrecor.com>.

The company is working to precisely identify and understand the factors that led to this situation. Once the company understands these factors, the company will evaluate the need for further action.

The authors of the PROACTION report published in the Journal of Emergency Medicine will submit a study update to the Journal once the data collected through the final expanded analysis are complete. Also, the PROACTION data included in the currently approved NATRECOR® product labeling do not include the two additional patient deaths. The company anticipates working with the FDA, as well as with relevant regulatory authorities in other countries, in coming weeks to determine the most appropriate way to ensure that these two cases are accurately reported as part of the full data set for this study.

PROACTION (Prospective Randomized Outcomes Study of Acutely Decompensated Congestive Heart Failure Treated Initially in Outpatients with NATRECOR®), an exploratory health outcomes pilot study, was a multi-center, randomized, double-blind, placebo-controlled trial evaluating the use of NATRECOR® as a treatment for acutely decompensated heart failure in patients treated in emergency rooms or observation units. The study treated 237 patients at 38 hospitals in the U.S. Patients were randomized to receive standard therapy plus NATRECOR®, or standard therapy plus placebo. PROACTION was designed to explore the clinical effects, safety profile and economic impact of the two treatment arms, and outcomes were assessed at 30 days following treatment. Dosing of NATRECOR® in this study was 2-mcg/kg intravenous bolus infusion, followed by a fixed-dose infusion of 0.01 mcg/kg/minute for a minimum of 12 hours, and a maximum of 24 hours.

About Scios Inc.

Scios Inc., a Johnson & Johnson company, is a biopharmaceutical company headquartered in Fremont, California. Scios is developing novel treatments for cardiovascular disease, inflammatory disease and cancer. The company's disease-based technology platform integrates expertise in protein biology with computational and medicinal chemistry to identify novel targets and rationally design small molecule compounds and peptides for markets with unmet medical needs. For more information, visit <http://www.sciosinc.com>.

#### IMPORTANT SAFETY INFORMATION

HYPOTENSION NATRECOR® (nesiritide) may cause hypotension and should be administered only in settings where blood

pressure can be monitored closely. If hypotension occurs during administration of NATRECOR® the dose should be reduced or discontinued. At the recommended dose of NATRECOR®, the incidence of symptomatic hypotension (4%) was similar to that of IV nitroglycerin (5%). Asymptomatic hypotension occurred in 8% of patients treated with either drug. In some cases, hypotension that occurs with NATRECOR® may be prolonged. The mean duration of symptomatic hypotension was longer with NATRECOR® than IV nitroglycerin (2.2 versus 0.7 hours, respectively). NATRECOR® should not be used in patients with systolic blood pressure <90 mm Hg or as primary therapy in patients with cardiogenic shock. The rate of symptomatic hypotension may be increased with a baseline blood pressure <100 mm Hg, and NATRECOR® should be used cautiously in these patients. In earlier trials, when NATRECOR® was initiated at doses higher than the 2 mcg/kg bolus followed by a 0.01 mcg/kg/min infusion, the frequency, duration, and intensity of hypotension was increased. The hypotensive episodes were also more often symptomatic and/or more likely to require medical intervention.

NATRECOR® is not recommended for patients for whom vasodilating agents are not appropriate and should be avoided in patients with low cardiac filling pressures.

## RENAL

NATRECOR® may affect renal function in susceptible individuals. In patients with severe heart failure whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, treatment with NATRECOR® may be associated with azotemia. In the VMAC trial, through day 30, the incidence of elevations in creatinine to >0.5 mg/dL above baseline was 28% and 21% in the NATRECOR® and nitroglycerin groups, respectively. When NATRECOR® was initiated at doses higher than 0.01 mcg/kg/min, there was an increased rate of elevated serum creatinine over baseline compared with standard therapies, although the rate of acute renal failure and need for dialysis was not increased.

## MORTALITY

In seven NATRECOR® clinical trials, through 30 days, 5.3% in the NATRECOR® treatment group died as compared with 4.3% in the group treated with other standard medications. In four clinical trials, through 180 days, 21.7% in the NATRECOR® treatment group died as compared with 21.5% in the group treated with other medications. There is not enough information to know if there is an increased risk of death after treatment with NATRECOR®.

SOURCE Scios Inc.

Mark T. Wolfe, office: +1-908-927-2745, cell: +1-908-672-4988, or

[mwolfe1@gpcus.jnj.com](mailto:mwolfe1@gpcus.jnj.com)

<http://www.prnewswire.com>