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**New Data Show Ferriprox Is More Efficacious Than Deferoxamine In Removing Iron From The Heart And In Preventing Early Death In Patients With Thalassemia**

**Dubai, UAE, 9 January 2006** – Results from two new studies demonstrate that treatment with the oral iron chelator Ferriprox™ (deferiprone) prevents iron-induced heart disease and significantly reduces the risk of early cardiac death in patients who undergo regular blood transfusions to treat thalassemia, a genetic disease that affects the body's ability to make red blood cells.

Thalassemia is a life-long condition requiring patients to have blood transfusions every 2-4 weeks, resulting in a build-up of toxic iron throughout the body including the heart, liver and endocrine glands. Data, published online in the journal *Blood* and presented this week at the annual meeting of the Thalassemia International Federation (TIF) in Dubai, show Ferriprox provides significantly better cardio-protection compared to deferoxamine (DFO), the current standard of care. Although DFO has improved survival rates among thalassemia patients, cardiac disease continues to be the most common cause of death, responsible for about 70 percent of deaths in DFO-treated patients, often in their second or third decade of life.<sup>1</sup>

Iron chelation is the only effective therapy for removing excess iron from the heart. Until recently, the only chelator available was DFO, a drug that must be injected under the skin for 8-12 hours, for 5-7 nights per week. Ferriprox, the first iron chelator which can be given by mouth, is currently approved in 48 countries, including the European Union, for the treatment of iron overload in patients with thalassemia major for whom deferoxamine therapy is contra-indicated or who present serious toxicity with deferoxamine therapy.

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<sup>1</sup> Borgna-Pignati C, Rugolotto S, De Stefano P, Zhao H, Cappellini MD, Del Vecchio GC, Romeo MA, Forni GL, Gamberinni MR, Ghilardi R, Piga A, Cnaan A. Survival and complications in patients with thalassemia major treated with transfusion and deferoxamine. *Haematologica*. 2004;89:1187-93.

**STUDY I DETAILS: Randomized Controlled Trial of Deferiprone or Deferoxamine in Beta-Thalassemia Major Patients with Asymptomatic Myocardial Siderosis<sup>2</sup>**

To better understand the benefits of Ferriprox versus DFO in reducing iron concentrations in the heart muscle (myocardial), researchers from the UK, Italy and Greece used Magnetic Resonance Imaging (MRI) to evaluate myocardial T2\*, an indicator of iron content in the heart, in sixty-one patients with beta-thalassemia major who were randomized to either continue treatment with DFO (32) or switched to Ferriprox (29). Previous research has demonstrated a strong relationship between low myocardial T2\*, indicating increased iron in the heart, and impaired ventricular function. The primary endpoint was the change in T2\* over one year.

Ferriprox was significantly more effective than DFO in reducing heart iron concentrations. The difference in removal of excess iron from the heart between Ferriprox and DFO was evident after only six months of therapy with an increase in T2\* of 18% for Ferriprox and 9% for DFO. After 12 months T2\* increased 27% and 13% respectively. In addition, there was a significant improvement in cardiac function, as measured by left ventricular ejection fraction (LVEF) in patients taking Ferriprox (3.1% absolute units) but not in those treated with DFO (0.3% absolute units).

“These results are exciting because they suggest that deferiprone has superior access to iron stores in the heart, which has important survival implications for this patient population,” said Dudley Pennell, M.D., lead investigator, Professor of Cardiology, Royal Brompton Hospital, London. “This cardio-protective benefit may be attributable to Ferriprox’s small, uncharged structure, providing a significantly greater potential to chelate intracellular iron in the heart.”

The most frequent adverse events reported in patients treated with Ferriprox were transient gastrointestinal symptoms (nausea, vomiting or abdominal pain). These usually occurred during the first week of treatment and resolved within a median of three days without discontinuation or a decrease in dose.

**STUDY II DETAILS: Cardiac Morbidity and Mortality in Deferoxamine- or Deferiprone-treated Patients with Thalassemia Major<sup>3</sup>**

In an epidemiologic, observational study conducted from January 1995 until December 2003, researchers at seven Italian thalassemia centers compared the occurrence of cardiac disease and deaths in patients with thalassemia major who were treated with either DFO or Ferriprox. Researchers collected demographic data, dates of cardiac complications and, when applicable, dates and causes of death.

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<sup>2</sup> Pennell DJ, Berdoukas V, Karagiorga M, Ladis V, Pgia A, Aesspoos A, Gotsis ED, Tanner MA, Smith GC, Westwood MA, Wonke B, Galanello R. Randomized Controlled Trial of Deferiprone or Deferoxamine in Beta-Thalassemia Major Patients with Asymptomatic Myocardial Siderosis. *Blood*. Prepublished online December 13, 2005.

<sup>3</sup> Borgna-Pignatti C, Cappellini MD, De Stephao P, Del Vecchio G, Forni G, Gamerini M, Ghilardi R, Piga A, Romeo M, Zhao H, Cnaan A. Cardiac morbidity and mortality in deferoxamine- or deferiprone-treated patients with thalassemia. *Blood*. Prepublished online December 22, 2005.

No cardiac-related events occurred in patients while treated with Ferriprox, while 52 cardiac events, including 15 cardiac-related deaths occurred in patients taking DFO.

Of the 516 patients enrolled in the study, 359 patients remained on DFO throughout the entire period, of which 14% developed a cardiac event, while none of the 157 patients who were switched to Ferriprox experienced a cardiac event.

Forty-six patients discontinued Ferriprox as a consequence of clinical or laboratory adverse events and 16 patients discontinued Ferriprox for reasons other than adverse events.

“Although DFO has been associated with a marked decrease in morbidity and mortality in chronically transfused patients, iron-induced cardiac disease continues to remain a serious problem,” said Caterina Borgna-Pignatti, M.D., lead investigator, Clinica Pediatrica of the University of Ferrara. “These findings support previous research demonstrating that the introduction of Ferriprox has significantly reduced the incidence of cardiac disease and actually limits early deaths in thalassemia patients.”

### **About Ferriprox**

The first iron chelator in Europe, which can be given orally instead of by injection, was Ferriprox™, approved in August 1999 as a second line therapy for patients with transfusion-dependent thalassemia. Since that time it has been used by thousands of patients in about 50 countries. Ferriprox (deferiprone) is administered in the range of 75-100 mg/kg/day in 3 equally divided doses and patients must be monitored weekly to detect early signs of a drop in white blood cells, secondary to agranulocytosis, which occurs in about 1% of patients. It works in conditions of iron overload, such as thalassemia, where frequent blood transfusions result in large deposits of iron in tissues, by binding to excess iron and removing it from the body, primarily in the urine. Effective chelation of iron in patients with iron overload decreases the risk of severe morbidity induced by excess iron in the tissues and prolongs survival as well. Full prescribing information is available from Apotex Inc.

### **About ApoPharma**

ApoPharma is the innovative drug development member of the Canadian-owned Apotex Group of Companies. ApoPharma is developing medications primarily in the fields of Iron Chelation and Wound Healing. Iron Chelation development has focused primarily in conditions of Iron Overload, such as thalassemia. Development in the field of Wound Healing has focused on the treatment of hard to heal wounds, such as those found in diabetic patients, where a proprietary product in final stages of development is based on human fibroblasts that generate new skin. The Apotex Group of companies plans to spend a total of \$1.3 billion over the next 10 years on research and development.

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