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Novartis Pivotal Study of Exjade® Shows Significant Reduction of Iron Overload in Patients with Non-transfusion-dependent Thalassemia

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- - Trial shows Exjade, an iron chelator, is significantly better than placebo at reducing liver iron concentration in patients with NTDT
- - Non-transfusion-dependent thalassemia (NTDT) is a genetic blood disorder in which patients may accumulate excess iron in the body
- - Data will serve as basis for first regulatory filings in US and Europe by year end

EAST HANOVER, N.J., Dec. 13, 2011 /PRNewswire/ -- Results from THALASSA, the first pivotal placebo-controlled study examining the benefit of iron chelation with Exjade® (deferasirox) in patients with non-transfusion-dependent thalassemia (NTDT), show that Exjade can significantly reduce iron overload. These data were presented today at the 53rd Annual Meeting of the American Society of Hematology in San Diego.

THALASSA investigated whether patients with NTDT and iron overload can benefit from iron chelation therapy as determined by liver iron concentration (LIC). The study met its primary endpoint, showing that Exjade at a 10 mg/kg/day starting dose significantly reduced LIC from baseline by 3.8 mg of iron per gram of liver dry weight (Fe/g dw) compared to an increase of 0.38 mg Fe/g dw in patients on placebo ($p<0.001$). The study also determined that a 10 mg/kg/day dose was superior to a 5 mg/kg/day dose ($p=0.009$).

In the 10 mg/kg arm, 49% of patients had a LIC decrease of at least 30% from baseline versus only 2% in the placebo arm. In addition, 56% of patients in the 10 mg/kg arm had a LIC decrease of greater than or equal to 3 mg at one year compared to 11% in the placebo arm. The most common adverse events reported were nausea, rash, diarrhea, headache and upper abdominal pain.(1) Adverse events were similar in all patient groups, including the placebo arm.(1)

Thalassemia refers to a diverse group of genetic disorders that affect red blood cell production, causing anemia. Unlike types of thalassemia in which patients require regular blood transfusions, NTDT patients can live without frequent transfusions. However, patients with NTDT are still at risk of accumulating excess iron.(2)

"Results from THALASSA show that Exjade is effective in reducing liver iron levels in patients with NTDT," said Ali Taher, the lead study investigator and Professor of Medicine, Division of Hematology and Oncology, American University of Beirut Medical Center, Lebanon. "Iron chelation therapy is the only option for decreasing these patients' iron burden. These are significant findings for patients with a major unmet need."(1)

NTDT refers to a group of clinically milder forms of thalassemias, including beta-thalassemia intermedia(3), Hemoglobin H disease (Hb H-alpha-thalassemia)(4) and Hemoglobin E/beta-thalassemia.(5) Despite a slower rate of iron accumulation, the burden of iron overload in NTDT patients is similar to that observed in thalassemia patients who receive regular blood transfusions. NTDT patients are not symptomatic at birth, when most thalassemias are diagnosed. Therefore they are often underdiagnosed and untreated even when symptoms appear at age 10 or later. NTDT is most commonly found in Southeast Asian, South Asian, Middle Eastern and Mediterranean populations.

"Over the past six years, Exjade has provided thalassemia patients an effective option for the treatment of chronic iron overload due to blood transfusions," said Herve Hoppenot, President, Novartis Oncology. "These new clinical trial data show that Exjade may also benefit NTDT patients who often are at risk for serious health complications."

Regulatory submissions for Exjade based on the THALASSA results are planned by the end of 2011.

Study details
The THALASSA study assessed the efficacy of Exjade versus placebo in NTDT patients greater than or equal to 10 years of age with iron overload.

THALASSA was a one-year, randomized, double-blind, placebo-controlled pivotal study, including 166 patients with beta-thalassemia intermedia (n=95), alpha-thalassemia (n=22) or Hemoglobin E/beta-thalassemia (n=49). Patients greater than or equal to 10 years of age with LIC greater than or equal to 5 mg Fe/g dw and serum ferritin >300 ng/mL were randomized to starting Exjade doses of 5 mg/kg/day (n=55) or matching placebo (n=28) and 10 mg/kg/day (n=55) or matching placebo (n=28).(1)

About Exjade
Exjade is indicated for the treatment of chronic iron overload due to blood transfusions (transfusional hemosiderosis) in adult and pediatric patients (aged 2 years and over). It is approved in over 100 countries including the US, Switzerland, Japan, and the countries comprising the European Union. The approved indication may vary depending upon the individual country.

Exjade Important Safety Information
Exjade is contraindicated in patients with creatinine clearance <40 mL/min or serum creatinine >2 times the age-appropriate upper limit of normal; poor performance status and high-risk myelodysplastic syndromes or advanced malignancies: platelet counts <50 x 109/L; known hypersensitivity to deferasirox or any component of Exjade.

There have been postmarketing reports of acute renal failure, hepatic failure, and cytopenias. Renal failure requiring temporary or permanent dialysis, renal tubulopathy, and interstitial nephritis have been reported. Upper gastrointestinal ulceration and hemorrhage, sometimes fatal, have been reported. Caution should be used in elderly patients due to a higher frequency of adverse reactions. Exjade is not recommended in patients with a short life expectancy (e.g., high-risk myelodysplastic syndromes), especially when co-morbidities could increase the risk of adverse events.

Skin rashes, serious hypersensitivity reactions, decreased hearing, and lens opacities have been reported. The most common adverse reactions are nausea, vomiting, diarrhea, abdominal pain, rash, non-progressive increases in serum creatinine, increased transaminases, abdominal distension, constipation, dyspepsia, proteinuria, and headache.

Please visit www.exjade.com for more information.

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The foregoing release contains forward-looking statements that can be identified by terminology such as "will," "may," "planned," or similar expressions, or by express or implied discussions regarding potential new indications or labeling for Exjade or regarding potential future revenues from Exjade. You should not place undue reliance on these statements. Such forward-looking statements reflect the current views of management regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results with Exjade to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Exjade will be

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About Novartis
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