

**Title: A Phase 2, 24 Week, Randomized, Open Label, Multi-Center Study to Assess the Safety, Tolerability, and Pharmacodynamics of FBS0701 in the Treatment of Chronic Iron Overload Requiring Chelation Therapy**

**IRB# 2010-042**

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**Synopsis:**

This is an open-label, 24 week study of two daily dose levels (16 and 32 mg/kg) of FBS0701. Each treatment arm will consist of approximately 20 patients with transfusional iron overload in need of chelation therapy.

Patients will be stratified according to historical transfusion requirements (high: >0.5 mg Fe/kg/d; low: <0.5 mg Fe/kg/d) and then randomized to one of two treatments (A: 16 mg/kg/d or B: 32 mg/kg/d).

Patients will be required to washout from their current chelation therapy for 2-5 days prior to dosing on Day 1. Patients will receive FBS0701 orally once daily for 24 weeks (approximately 6 months). At the conclusion of the dosing period, patients will washout from study drug for 1 week prior to resuming their previous chelation therapy. Patients will undergo an End-of-Study (EOS) visit at Week 28.

Approximately forty adult patients with documented transfusional iron overload between the ages of eighteen and sixty years will be studied. The use of only adults with transfusional iron overload is considered appropriate because the safety of FBS0701 has not been studied in non-clinical/nonclinical models at pre-adult ages. To lower the likelihood of over-chelation or under-chelation, investigators will limit the study population at the time of first dose to those with liver iron concentration (LIC) equivalent of between  $\geq 3.5$  and  $\leq 30$  mg iron per g (dry weight) and those patients with a serum ferritin >500 ng/mL.

Patients in this study may have the following primary diagnoses: hereditary anemias such as sickle cell disease,  $\beta$ -thalassemia, and Diamond-Blackfan anemia; acquired anemias such as myelodysplastic syndrome and other forms of bone marrow failure. Patients with iron overload from causes other than transfusional hemosiderosis will be excluded from this study.

Safety will be assessed in clinic, weekly for Weeks 1-4 of therapy, bi-weekly for Weeks 6-8, moving to every 4 weeks during Weeks 12-24. Safety assessments will consist of adverse event recording, vital signs measurements, blood sampling, urinalysis, physical examinations, and ECGs.

Pharmacodynamic (PD) parameters will be assessed by a FerriScan® abdominal MRI. For research purposes and on a voluntary basis, a blood sample will be collected from consenting patients for exploratory analysis of genetic and expression variations related to transfusional iron overload and the effects of FBS0701.