AN ADAPTIVE, RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND, MULTI-CENTER STUDY OF ORAL FT-4202, A PYRUVATE KINASE ACTIVATOR, IN PATIENTS WITH SICKLE CELL DISEASE (SCD)

Purpose
The primary purpose of the Hibiscus Study™ is to assess the safety and efficacy of the once-daily oral investigational medication FT-4202 in adolescents and adults with SCD compared with placebo. Efficacy will be measured by hemoglobin (Hb) response and annualized vaso-occlusive crisis (VOC) rate.

Design
This is a phase 2/3 study in which the first 60–90 participants will be randomized to receive one of two dose levels of the once-daily oral investigational medication FT-4202 or a placebo, followed by up to 274 participants receiving the optimal dose of FT-4202 or placebo. All participants who complete the double-blind study treatment period may be eligible to continue in the open-label extension period. Up to 344 total participants will be enrolled in the study at approximately 75 sites around the world.

Study duration
The total duration of the study for each participant is approximately 113 weeks. This includes screening (up to 5 weeks), double-blind study treatment (up to 52 weeks), open-label extension study treatment (up to 52 weeks), and an end-of-study visit 4 weeks after the last dose of the investigational medication. The maximum study treatment period for a participant is 104 weeks.

Eligibility criteria
Key inclusion criteria
- Ages 12 to 65 years, inclusive, at time of randomization.
- Patient has a confirmed diagnosis of SCD.
- Documentation of SCD genotype (HbSS, HbSβ⁰-thalassemia, or other sickle cell syndrome variants) based on prior history of laboratory testing; if unavailable, must be confirmed by laboratory testing during screening.
- Patient has had at least 2 episodes of VOC in the past 12 months.
- For study eligibility, VOC is defined as a previously documented episode of acute chest syndrome (ACS) or acute painful crisis (for which there was no explanation other than VOC) that required prescription or healthcare professional–instructed use of analgesics for moderate to severe pain (documentation must exist in the patient medical record prior to screening).
- For participants taking hydroxyurea (HU), the dose of HU (mg/kg) must be stable (no more than a 20% change in dosing) for at least 90 days prior to start of study treatment with no anticipated need for dose adjustments during the study, in the opinion of the investigator.

Key exclusion criteria
- More than 10 VOCs within the past 12 months.
- Hospitalized for sickle cell crisis or other VOC event within 14 days of signing the informed consent form.
- Female who is breastfeeding or pregnant.
- Patients with clinically significant bacterial, fungal, parasitic, or viral infection requiring systemic therapy.
- Patients with acute bacterial, fungal, parasitic, or viral infection requiring systemic therapy should delay screening/enrollment until active therapy has been completed.

Thank you for your interest in the Hibiscus Study. For more information or to refer a patient, please visit HibiscusSCTrial.com.