SANGUINATE® Promotes Return of Deoxygenated Sickle Cell RBCs to a Normal Morphology in Patients with Vaso-Occlusive Crisis

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SANGUINATE® is a carbon monoxide/oxygen delivery agent in clinical development for indications wherein low oxygen availability plays a pathological role. SANGUINATE® has demonstrated the ability to “unsickle” red blood cells (RBCs) in ex vivo studies. A Phase II study (NCT02411708) is ongoing for the treatment of sickle cell disease (SCD) patients in severe Vaso-Occlusive Crisis (VOC). An interim analysis was conducted to ascertain the ability of SANGUINATE® to return sickled RBCs to a more normal “round” morphology.

Participants were randomized to SANGUINATE® or a placebo, in addition to standard treatment and IV opioid per institutional practice. Blood samples were collected pre-infusion, at the time of discharge, and 72 hours after infusion. Samples were shipped by priority overnight, and analyzed for reversal of sickling by imaging cytometry and shape analysis.

Clinical trial samples from SCD patients receiving SANGUINATE® showed a shape-shift back to a round morphology that was not observed in the placebo arm. Importantly, the reversal occurred rapidly within hours of the infusion and persisted through the 72hr time point.

VOC occurs due to the obstruction of the microvasculature by deoxygenated SCD RBCs and the effects of inflammatory mediators. The unique gas transfer properties of SANGUINATE®-deoxygenated SCD RBCs and the effects of inflammatory mediators are ongoing for the treatment of sickle cell disease (SCD) patients in severe Vaso-Occlusive Crisis (VOC). (NCT02411708). The unique gas transfer properties of SANGUINATE®-deoxygenated SCD RBCs and the effects of inflammatory mediators were studied in SCD patients receiving SANGUINATE®. RBC morphology in SANGUINATE®-treated VOC patients. Studies in patients with stable SCD and in patients with leg showered a shape-shift back to a round morphology in SANGUINATE®-treated VOC patients. These data support the continued evaluation of SANGUINATE® in VOC patients. Future analysis will focus on the relationship between unsickling and pain reduction.

SANGUINATE® What is it?

SANGUINATE® Active O2 Transfer Mechanism

**SANGUINATE® MOA Applies to Tissues AND RBCs**

**Clinical Study**

**Study of SANGUINATE® in the Treatment of Sickle Cell Disease Patients with Vaso-Occlusive Crisis**

- Purpose
  - Phase II, randomized (2:1) ratio, placebo-controlled, single-dose, single-blind study in ambulatory settings (i.e. inpatient acute care, ED, hospital study)
  - 2-hour IV infusion period
  - Estimated enrollment: 24 adult participants
  - Primary Outcome Measure: Time to readiness for discharge from ambulatory site

- Secondary Exploratory Observations: Blood Morphology, Markers of inflammation and adhesion

- Blood samples are being collected (prior to infusion, at time of discharge and 72-hours post discharge) to assess the impact of SANGUINATE® on RBC morphology and inflammatory markers.

**VOC-OCO® Controlled Treatment Shifts the Sickle/Unsickle Ratio**

- Phase II VOC Study: Measurement of In vivo Unsickling by Imaging Cytometry

- Rapid Reversal Upon SANGUINATE® Addition

  - RBCs from a SCD (HbSS) volunteer were cultured under hypoxic conditions. SANGUINATE® was added in a directional distribution to observe effects on sickling. Video images were captured with still-frame exposures shown here.

- SANGUINATE®® Promotes Reversal of Sickled Cell RBC Morphology

- In Vitro Reversal of Sickled Cell RBCs Morphology Visualizing Effects via Microscopy

- **In Vitro SCD RBC Unsickling by Imaging Cytometry**

- **Automated Unsickling RBC In Vitro**

- **Quantitative Evidence of Effects**

For More Information Please Contact: www.prolongpharma.com

The Conflict of Interest disclosure forms for above authors have been satisfied.

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**SANGUINATE®® Promotes Return of Deoxygenated Sickle Cell RBCs to a Normal Morphology in Patients with Vaso-Occlusive Crisis**

**SANGUINATE®® In Vivo Gas Transfer to Isolated RBC**

- **In Vitro Reversal of Sickled Cell RBCs Morphology Visualizing Effects via Microscopy**

- **Ex Vivo SCD RBC Unsickling by Imaging Cytometry**

- **SANGUINATE®® Controlled Treatment Shifts the Sickle/Unsickle Ratio**

- **Secondary Exploratory Observations: Blood Morphology, Markers of inflammation and adhesion**

- **Quantitative Evidence of Effects**

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