**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 occur due to the obstruction of the microvasculature by deoxygenated SCD RBCs and the effects of inflammatory mediators. The unique gas transfer properties of SANGUINATE® resulted in the rapid delivery of oxygen to hypoxic RBCs promoting a shape-shift to a more normal round morphology in SANGUINATE®-treated VOC patients. Studies in patients with stable SCD and in patients with leg have shown this product to be well tolerated in patient population. These data support the continued evaluation of SANGUINATE® in VOC patients. Future analysis will focus on the relationship between unsickling and pain reduction.