

# Sanguinate™: A CO/O<sub>2</sub> delivery therapeutic for the treatment of anemic and ischemic disorders

*Abraham Abuchowski, PHD.*

*Prolong Pharmaceuticals. South Plainfield NJ. Email:abe@prolongpharma.com*

**Background:** Historically, blood substitutes were under development that would provide oxygen carrying capacity as well as fluid replacement for both trauma and surgical indications. Their development was halted by the inability of the products to deliver therapeutic amounts of oxygen targeted to hypoxic tissue as well as the inherent toxicity of the molecules. This led to the concept of an oxygen therapeutic which would be targeted towards indications due to anemia and ischemia but not exhibit the toxicity that plagued earlier products. The complex pathophysiology of disease such as sickle cell and hemorrhagic stroke, not only have hypoxia as a pivotal event but inflammation and vasoconstriction that perpetuate the oxygen deprivation. There is, therefore, a need for an effective therapeutic that addresses the multiple events of inflammation and oxygen deprivation.

**Methods:** Prolong Pharmaceuticals has developed a pegylated carboxyhemoglobin therapeutic, SANGUINATE, which acts as a dual mode carbon monoxide (CO) and oxygen delivery therapeutic. It has been designed with a p50 value that optimizes transfer of oxygen to hypoxic tissue. Infusion of this product results in the release of the CO molecule as the anti-inflammatory agent and the consequent repeated transfer of oxygen. Extensive preclinical studies as well as ongoing clinical trials substantiate the mechanism of action and safety of SANGUINATE.

**Results:** *In vitro* and *in vivo* studies have demonstrated the ability of the released CO to down regulate inflammatory mediators known to play a role in tissue damage and occlusion of blood vessels. Experiments have also demonstrated the ability of SANGUINATE to deliver oxygen to hypoxic tissue. Using red blood cells from sickle cell disease patients, SANGUINATE has been shown to alter the morphology of the cells to a more normal shape which could only occur when the hemoglobin SS molecules are oxygenated. Findings from multiple animal toxicity studies in mice, rats, pigs, and non-human primates have revealed no serious adverse physiological, histological, or immunological effects from repeat infusions with SANGUINATE, even at doses up to 1200 mg/kg (monkey), 1600 mg/kg (pig), and 2400 mg/kg (rat). First-in-human studies of multiple doses of SANGUINATE in healthy adults and in Sickle Cell Disease patients (80, 120, 160, and 320 mg/kg) have also been completed, revealing no drug-related serious adverse effects while showing clear dose-dependent pharmacokinetics. Efficacy of SANGUINATE is currently under clinical investigation in patients with delayed cerebral ischemia following subarachnoid hemorrhage, Sickle Cell crisis, Sickle Cell leg ulcers, allosensitized patients undergoing renal dialysis and for pulmonary hypertension in beta thalassemia patients. In addition, 6 patients with life-threatening anemia (Hb levels <3.5g/dL) have been treated under emergency INDs

**Conclusion:** In addition to its oxygen therapeutic capability, SANGUINATE also acts as a CO-releasing molecule, thereby not only improving its ability to treat or prevent hypoxia but also to act upon concurrent pathologies such as inflammation and reperfusion injury. This expands the potential therapeutic utility of SANGUINATE beyond anemia into indications such as early brain injury and delayed kidney graft function where inflammation plays a pivotal pathological role as well as in indications such as sickle cell disease where the inflammation and hypoxia contribute

to the development of comorbidities such as vaso-occlusive crisis. Clinical trials are underway in a number of indications with results anticipated in 2015.

Key-words: oxygen therapeutic, oxygen carrier, SANGUINATE, anemia.