**Abstract**

Peripheral vascular disease (PVD) affects approximately 12 million Americans and is associated with significant morbidity and mortality. PVD prevalence increases dramatically with age, affecting approximately 20% of Americans age 65 and older. Patients with advanced PVD who are ineligible for reconstruction or in whom prior revascularization has been unsuccessful have 6-month amputation and mortality rates as high as 40% and 20%, respectively. Despite its prevalence and cardiovascular risk implications, only 20 to 30 percent of PVD patients are undergoing treatment. JVS-100 comprises a non-viral DNA plasmid engineered to transiently express human Stromal cell Derived Factor 1 (SDF-1). SDF-1 is a strong chemoattractant of endogenous organ specific and bone marrow derived stem cells and progenitor cells to the site of tissue damage, which promotes tissue preservation and blood vessel development. JVS-100 is based on a novel plasmid expression system manufactured by Aldevron LLC (North Dakota).

**Background**

**Peripheral vascular disease**

- Affects 1% of Americans over 50 (>1 million in US)
- 1 yr mortality rate of patients with CLI is 25%
- Only 30-50% of patients are undergoing treatment, of which 30% may require amputation
- 150,000 amputations per year in the US

Critical limb ischemia (CLI) in the US

- 125,000-250,000 patients per year
- Affects 1% of Americans over 50 (~1 million in US)
- 1 yr mortality rate of patients with CLI is 25%
- Only 30-50% of patients are undergoing treatment, of which 30% may require amputation
- 150,000 amputations per year in the US

SDF-1

- Also known as CXCL12
- 8 kDa chemokine, receptor is CXCR4
- Expressed in most tissues, including skin
- Improves cardiac function after acute myocardial infarction
- Mobilizes/maintains hematopoietic stem cells to injured tissues
- SDF-1 is increased in wounds after trauma
- SDF-1 therapy in diabetic wounds increased healing
- Increased SDF-1 expression stimulates blood vessel formation in damaged tissue

**Hypothesis:**

Direct injection of JVS-100 to increase SDF-1 expression in a rabbit model of hind limb ischemia will increase blood flow.

**Results**

**JVS-100 expresses hSDF-1 and induces dose-dependent MSC migration**

**SDF-1 stimulated vasculogenesis in ischemic rabbit hindlimbs**

**Summary and Conclusions**

- JVS-100 expresses functional SDF-1 which induces MSC migration
- Peak SDF-1 expression occurs 3 days post muscle injection
- 8 injections of 1 or 2 mg/mL JVS-100 induced therapeutic benefit
- JVS-100 increased angiogenic score 30 and 60 days post-injection (p < 0.05 vs. control). Data shown as average +/- SEM.
- Direct injection of JVS-100 improves angiogenesis in rabbits with CLI.

**References:**