Background

**SDF-1**

- Also known as CXCL12
- 8 KDa chemokine, receptor is CXCR4
- Upregulated in damaged tissue, including skin
- Improves cardiac function after acute myocardial infarction
- Mobilizes/recruits hematopoietic stem cells to injured tissue
- SDF-1 is increased in wounds after trauma
- SDF-1 therapy in diabetic wounds increased healing

**Hypothesis**

- Re-introducing SDF-1 expression in a chronically damaged heart using naked plasmid DNA gene transfer will increase cardiac function.

Results

**JVS-100 Improves 6MWD at 4 and 12 Months**

*Figure 3. JVS-100 causes improvement in 6MWD at 4 and 12 months. Improvements in the 15 and 30 mg dose groups combined was statistically significant over baseline (median 36 m, p=0.002). At 12 months, there was a 12 m difference between the 5 and 15 mg dose groups, but maintained improvement in the 30 mg dose group.

**Results**

**SDS as Measured by SPECT**

*Figure 5. JVS-100 causes stabilization of SDS. There was an increase in SDS from baseline to 4 months in the 5 mg group. When the change in SDS in the 5 mg group was compared to the combined 15 and 30 mg group, the difference was statistically significant.

Adverse Event Summary Ctd.

- One patient experienced vomiting and diarrhea, which was reported as "possibly related" to study drug. This event was not serious.
- One subject was diagnosed with systemic lupus erythematosus 16 days after receiving the study drug, however analysis of stored blood samples revealed that the subject had a positive ANA titers (1/320) with a positive background, but no history of SLE.
- All subjects experienced a short-term elevation in cardiac enzymes 6-18 hours after the injection. There were no associated cardiac symptoms reported with these enzyme changes.

Summary and Conclusions

**Key safety and efficacy findings of the Phase I Dose-Escalation Study**

- JVS-100 was safe and well-tolerated at all doses studied and the primary safety endpoint was met with no adverse events likely related to the drug.
- Injection of 15 and 30 mg doses of JVS-100 improved QOL, 6MWD, and NYHA at 4 and 12 months in NYHA Class III heart failure patients.
- These data served as the basis for a randomized, placebo-controlled 90 patient, Phase II trial (STOP-HF, NCT 01843510) at 12 US clinical sites. In STOP-HF, symptomatic ischemic HF patients are randomized to placebo, 15 mg JVS-100, or 30 mg JVS-100 and the safety and efficacy of JVS-100 will be tested.

References:


**Observations**

- 26 SAEs were reported in subjects that received study drug. Only 1 SAE (worsening heart failure) was thought to be “possibly related” to JVS-100. No other SAEs or adverse events reported as “related” or “possibly related” to JVS-100.