**BACKGROUND**
- HF-10 is a naturally mutated strain of herpes simplex virus 1 (HSV-1).
- HF-10 is replication-competent and exhibits attenuated neuro-invasiveness due to several genomic deletions and insertions.
- In vivo oncolytic activity has been demonstrated in various solid tumor models.
- HF-10 has also demonstrated systemic anti-tumor activity via activation of tumor immunity.
- HF-10 intratumoral treatment has been well-tolerated in human studies conducted in Japan.

**STUDY OBJECTIVES**
- Assess safety and determine recommended dose for further studies.
- Characterize changes in HF-10 replication in body fluids.
- Assess anti-tumor activity and intratumoral viral replication.
- Evaluate antitumor lymphocyte response and identify serum biomarkers of antitumor activity.

**STUDY DESIGN**
- Open-label, multi-center dose escalation study evaluating both single and repeat intratumoral dosing with HF-10 injection.
- Study has a 7-3-15 design with 4-dose escalation scheme.
- Starting dose of HF-10 in Stage I is 1 x 10^6 TCID50/dose with incremental dose escalations of 5 x 10^6 TCID50/dose, 1 x 10^7 TCID50/dose, and 1 x 10^8 TCID50/dose.
- Stage II is evaluating multiple dosing at 1 x 10^6 TCID50/dose or 1 x 10^7 TCID50/dose (Figure 1).

**RESULTS**
- A total of 21 patients have been enrolled to date, of which 19 patients with various tumor types have been treated (Table 1).
- In Stage I, 1 x 10^6 TCID50/dose, no dose limiting toxicities nor any Serious Adverse Events related to HF-10 therapy were observed.
- One HSV-1 seronegative patient has been treated in Stage II.
- Patient demonstrated a 20% decrease in the longest diameter of the injected lesion.

**CORRELATIVE STUDY RESULTS**
- Peripheral blood from 13 patients treated in Stage I drawn at pre-HF-10 administration and post-injection Day 15.
- Multicolor flow cytometry performed on patient lymphocytes using antibodies for CD3, CD4, CD8, CD14, CD16, CD20, CD56, CD25, CD11c, CD14, TGF-beta (LAP), and Foxp3, as well as flexible viability dye exclusion (to exclude dead cells).
- Luminex 30-plex assay performed on patient serum according to manufacturer’s specifications.

**CONCLUSIONS**
- Treatment with intratumorally-injected HF-10 has been well-tolerated in multiple types of solid tumor malignancies and in patients who are both naïve or who had previous exposure to HSV-1.
- There appears to be a significant I-6 related inflammatory response to treatment along with increased peripheral monocytes.
- Patients 10 and 11 responded strongly along both of these axes, though this did not correlate with clinical response.
- Decreased CD8+PD1+ cells may indicate a shift towards a non-exhausted functional CD8 phenotype, or homing of naive PD1+ cells to the injected tumor.