**Abstract**

**BACKGROUND:** Optimized new therapies for HCV are needed that have pan genotypic activity and a high barrier to viral resistance. To meet these challenges, 3-V Biosciences has developed a small molecule inhibitor of HCV that targets the host’s fatty acid synthase (FASN) enzyme (Abstract 88). HCV infection increases the expression of FASN, the host enzyme responsible for the production of palmitate, and down regulation of FASN inhibits critical viral processes including entry into cells, RNA replication, and particle assembly. FASN inhibitors are expected to have pan-genotypic activity and pose a high barrier to viral resistance due to interference with the HCV lifecycle.

**OBJECTIVE:** The objective of this study is to characterize the pharmaceutical properties of a novel, small molecule inhibitor of FASN as a treatment for chronic HCV infection.

**RESULTS:** 3-V Bioscience’s FASN small molecule inhibits the human FASN enzyme in biochemical and cell based assays with an EC$_{50}$ of 0.060 µM and no observed cytotoxicity. A 10 mpk oral dose of this compound is rapidly absorbed and highly bioavailable (~60%) in rats and dogs with an apparent half-life of 3.2 h and 3.9 h, respectively. Pharmacodynamic activity in rats is exposure-dependent: a 60 mpk dose causes complete inhibition of palmitate synthesis 12h after administration while a single 30 mpk oral dose causes ~50% inhibition at 12h. Palmitate synthesis remains suppressed by ~60% at 24 hours following a 60 mpk dose, consistent with a once-daily oral dosing regimen. The results of this current work demonstrate that 3-V Bioscience’s FASN inhibitor can inhibit de novo fatty acid synthesis in vivo and has pharmaceutical properties necessary for clinical development.

**Conclusions**

- A single oral dose can inhibit de novo palmitate synthesis up to 24 hours in vivo
- Inhibition is reversible in vivo
- Reduction of de novo palmitate synthesis correlates with liver concentration of the drug
- The drug’s profile meets the criteria to advance into Phase 1 clinical studies in 2013

**Disclosures:** All authors are current or former employees of 3-V Biosciences, Inc.