INTRODUCTION

- Tenofovir Exalidex (TXL) has been investigated clinically in phase 1 and 2 clinical trials. TXL was well tolerated and, in a phase 2 trial consisting of 62 patients, mean viral load reduction was approximately 3 logs after QD oral administration of 50-100 mg for 28 days.
- The solid dosage formulation of TXL was examined in detail and it was determined that further optimization of the tablet was possible, owing to the physicochemical properties of TXL.
- Prior to embarking on further testing of novel formulations in humans, a canine study was undertaken to determine possible improvements in formulation, including disintegration, dissolution/solubility and oral delivery. Herein, is described the pharmacokinetics of TXL in a dog model to evaluate five different test formulations, compared to a reference.

Tenofovir Exalidex (TXL)

“Lipid” tail chemically modified tenofovir designed to target liver.

- TXL is designed to mimic lysophosphatidylcholine to take advantage of natural lipid uptake pathways and achieve high hepatic intracellular concentrations, while minimizing high circulating levels of TFV.
- TXL orally available as a once daily tablet.
- Physicochemical properties of TXL include: highly water soluble, 7.41 calculated LogP, and high liver extraction minimizing high circulating levels of TFV.

Results

- A total of 24 beagle male dogs weighing between 8-12 kg were administered one of 6 possible formulations.
- Single oral dose of TXL (n=4 dogs/group)
- Blood collected into EDTA tubes.
- Plasma determinations using LC-MS/MS.

Results continued

- The pharmacokinetics of TXL was determined for all six TXL formulations in beagle dogs.
- Formulation A was used in a previous clinical trial of TXL administered to chronic HBV patients.
- Formulation D, thus far, appeared to have the more favorable PK profile as indicated by mean increases in both AUC and Cmax.
- All 5 formulations had greater AUC values compared with the reference.
- Only one formulation had a slightly lower Cmax compared with the reference.

DISCUSSION AND CONCLUSIONS

- TXL is a novel lipid-conjugated prodrug of tenofovir that confers altered physicochemical properties relative to existing commercial versions of tenofovir.
- Unique physicochemical properties may be exploited to further optimize TXL formulation (e.g., logP, aqueous solubility, polar surface area).
- Canine model suggests that TXL formulation may be further studied in chronic HBV patients.