Gemcabene is a novel lipid-regulating compound being developed as an adjunct to diet and statin therapy for the treatment of dyslipidemia. Gemcabene was administered in a randomized, double-blind, rising, multiple-dose safety, tolerance, pharmacokinetic, and pharmacodynamic study in healthy subjects. Gemcabene’s dual mechanism of action is designed to enhance the clearance of very low-density lipoprotein-cholesterol (VLDL-C), a rare genetic lipid disorder which results in elevated LDL-C usually due to mutations in one allele of the LDL receptor gene, and (ii) abnormally high triglycerides (TGs), a more prevalent genetic lipid condition which results in elevated LDL-C, usually due to mutations in one allele of the LDL receptor gene, and (iii) abnormally high triglycerides (TGs).

Gemcabene is rapidly absorbed with dose proportional increases in maximum plasma concentration (Cmax) and area under plasma concentration-time curve (AUC) from 0 to 24 hours (AUC(0-24)) values. Elimination half-life values were independent of dose and averaged 49 hours across all dose levels. Gemcabene is rapidly absorbed with dose proportional increases in maximum plasma concentration (Cmax) and area under plasma concentration-time curve (AUC) from 0 to 24 hours (AUC(0-24)) values. Elimination half-life values were independent of dose and averaged 49 hours across all dose levels. Gemcabene is rapidly absorbed with dose proportional increases in maximum plasma concentration (Cmax) and area under plasma concentration-time curve (AUC) from 0 to 24 hours (AUC(0-24)) values. Elimination half-life values were independent of dose and averaged 49 hours across all dose levels.

As presented in Figure 6, gemcabene significantly lowered LDL-C with a mean percent change of approximately -30% from 450 mg to 900 mg. While Figure 4 might suggest an effective dose may be 450 mg to 900 mg, a closer review of dose response by exposure (μg/mL/day) suggests the 600 mg dose would be the most appropriate dose covering the range of 6-12 μg/mL for the broadest subject population (Table 1).

As presented in Figure 5 and 6, gemcabene LDL-C lowering exceeds 20% when AUC(0-24) values are greater than 2500 hr μg/mL with limited additional LDL-C lowering above 5000 hr μg/mL.

**CONCLUSIONS**

Gemcabene is rapidly absorbed following administration, with time occurring within 2 hours of dosing. Both Cmax and AUC were approximately dose proportional following both single- and multiple-dose administration. Multiple dosing QD resulted in a consistent 12-fold of approximately 32 to 48 hours, and minimal accumulation was observed following 4 weeks of dosing. Gemcabene’s primary route of elimination is renal.

Gemcabene was well tolerated and was observed to significantly lower total cholesterol, LDL-C and ApoA at once daily doses of 450 to 900 mg. Gemcabene is being developed as an oral, lipid-altering agent to be used as an adjunctive therapy for the treatment of dyslipidemia, including the rare indication of HoFH.

**REFERENCES**

* 3027-001 - An Oral, Rising, Multiple-Dose Tolerance, Pharmacokinetic and Pharmacodynamic Study of Gemcabene Capsules in Healthy Volunteers (clinicaltrials.gov identifier: NCT02587364)