GRX-917 – Superior Pharmacokinetic Profile to Etifoxine

A) In-Vitro: Liver Microsome Stability

	Etifoxine $t_{1/2}$ (mins)	GRX-917 $t_{1/2}$ (mins)
Rat	7.6	13.8 (+82%)
Human	22.4	40.8 (+82%)

GRX-917's half-life in human and rat liver microsomes is increased by 82%. In rats, this enhanced *in-vitro* metabolic stability translates *in-vivo* to a 1.7 fold increase in maximum concentration (Cmax) and a 2.5 fold increase in exposure (AUC) for the GRX-917 compared to etifoxine. Terminal half-life was also increased by 20%.

These results are consistent with predominantly decreased pre-systemic metabolism, resulting in higher bioavailability and also reduced systemic clearance, increasing the drug's half-life.

The effect of deuterium substitution on enhancing microsome stability is identical (+82%) in rats and humans, pointing to a similar metabolic pathway. Therefore, GRX-917's superior rat pharmacokinetic profile is expected to translate to humans in a similar fashion.

B) In-Vivo: Oral 50 mg/kg dose in Sprague-Dawley Rats