

Property	Acceptable	Preferable
Mechanism of action		
Functional selectivity	> 30X	>100X
Cellular Activity	< 5uM	< 1uM
In vivo efficacy		
Protein Binding	<99%	<95%
Solubility	>3uM at pH 1.5-3, >1 pH 7.4	>10uM at pH 1.5-3, >5 pH 7.4
Cyps, particularly 3A4 and 2D6	<50% at 10uM	<50% at 30uM
Microsomes: % 60 min	Human >80%, cyno and rat >60%	Human >85%, cyno and rat >70%
Bioavailability rat, cyno/dog	rat >10%, cyno >20%	Rat >20%, cyno>40%
Half life, hours	>1h rat, >1.5h cyno, >1.5 dog	>1.5h rat, >2h cyno, >2h dog
Metabolites	Rat/cyno/dog have human metabolites	
Ames and micronucleus	Negative	Negative
hERG	Negative at 20x EC50	Negative at 50X EC50
Cerep Profile	No limiting pharmacology	No limiting pharmacology
Multiple dose tolerance	No issues at 5X expected dose	None at 10X
Caco2 Permeability A-B	10	20
Caco2 efflux ratio	<8	<5
Ratio PD dose / AE dose	>10	>30 (depends on AE)