

Table S2. Targeted properties for *T. cruzi* and *Leishmania* spp as set by GHIT, and our established criteria for *T.b. brucei* [1, 2]

		<i>T. cruzi</i>	<i>Leishmania</i> spp.	<i>T. brucei</i>
Potency	EC ₅₀ LLE (pEC ₅₀ – cLogP)	<10 μM	<10 μM	<1 μM ≥4
<i>In vitro</i> Toxicity	HepG2 TC ₅₀ 3T3 TC ₅₀	≥10 x EC ₅₀ ≥10 x EC ₅₀	≥10 x EC ₅₀ ≥10 x EC ₅₀	≥10 x EC ₅₀ ≥10 x EC ₅₀
ADME	Molecular Weight (g/mol) cLogP LogD RH Cl _{int} HLM Cl _{int} Aqueous Solubility (μM) Plasma Protein Binding (%)	Adherence to 'rule of five' preferred	Adherence to 'rule of five' preferred	≤360 ≤3 ≤2 ≤27 ≤47 >10 ≤95
Efficacy		>80% reduction in parasite burden after 10 doses at 50 mg/kg (PO)	>70% reduction in liver parasite burden after max 5 doses at 50 mg/kg (PO; QD, BID)	Reduction, control, or elimination of parasitemia following PO or IP dosing

References

1. Lipinski, C. A.; Lombardo, F.; Dominy, B. W.; Feeney, P. J., Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. The article was originally published in *Advanced Drug Delivery Reviews* 23 (1997) 3–25.1. *Advanced Drug Delivery Reviews* **2001**, 46 (1), 3-26.
2. Katsuno, K.; Burrows, J. N.; Duncan, K.; van Huijsduijnen, R. H.; Kaneko, T.; Kita, K.; Mowbray, C. E.; Schmatz, D.; Warner, P.; Slingsby, B. T., Hit and lead criteria in drug discovery for infectious diseases of the developing world. *Nat Rev Drug Discov* **2015**, 14 (11), 751-758.