This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Infectious disease				
Leishmaniasis; African sleeping sickness	Pteridine reductase (PTR1); dihydrofolate reductase (DHFR)	*In vitro* studies suggest that simultaneously antagonizing two folate reductase enzymes, PTR1 and DHFR, could be more useful for treating *Leishmania major* and *Trypanosoma cruzi* infections than antagonizing DHFR alone. When combined with known DHFR inhibitors, several quinoxaline and diaminopteridine PTR1 inhibitors additively reduced the growth of both wild-type and PTR1-overexpressing *L. major* and *T. cruzi* strains. Next steps include combining the inhibitors, determining *in vivo* toxicities and testing the compounds against other parasites. Iclaprim (AR-100), a broad-spectrum DHFR inhibitor from Arpida Ltd., is in clinical development to treat malarial infection as well as bacterial infections including pneumonia and skin and skin structure infections. The DHFR inhibitor CDA, a fixed-dose combination of chlorproguanil hydrochloride, dapsone and artesunate from GlaxoSmithKline plc, is in a Phase III trial to treat malaria.	The inhibitors are patented by Maria Paola Costi in Italy as antiparasitic agents; unavailable for licensing	Cavazzuti, A. *et al. Proc. Natl. Acad. Sci. USA*; published online Feb. 1, 2008; doi:10.1073/pnas.0704384105 Contact: Maria Paola Costi, Università di Modena e Reggio Emilia, Modena, Italy e-mail: stuart_orkin@dfci.harvard.edu