This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Cancer				
Gastrointestinal cancer	Stem cell factor receptor tyrosine kinase (c-Kit; KIT; CD117)	<p><i>In vitro</i> studies suggest quinazoline-pyrazolourea-based KIT inhibitors could help treat Gleevec imatinib-resistant gastrointestinal stromal tumors (GISTs). Chemical synthesis, SAR and <i>in vitro</i> testing identified quinazoline-pyrazolourea analogs that inhibited wild-type KIT and two imatinib-resistant KIT mutants with low nanomolar IC₅₀ values. In human GIST cell lines expressing constitutively active KIT or the imatinib-resistant T670I KIT mutant, 3 of the lead compounds caused 50% growth inhibition at low nanomolar concentrations. Future studies could include testing the lead compounds in animal models bearing imatinib-resistant GIST xenografts. Novartis AG markets Gleevec, a BCR-ABL tyrosine kinase inhibitor, to treat GISTs, acute lymphoblastic leukemia (ALL), chronic myelogenous leukemia (CML) and other hematological malignancies. The drug also is under review for hypertension and in Phase II testing to treat melanoma and scleroderma. AB Science S.A.'s KIT inhibitor masitinib is under review for imatinib-resistant GISTs and in Phase III testing to treat other cancers.</p> <p>SciBX 6(28); doi:10.1038/scibx.2013.716 Published online July 25, 2013</p>	Patent and licensing status unavailable	<p>Richters, A. <i>et al. J. Med. Chem.</i>; published online June 17, 2013; doi:10.1021/jm4004076</p> <p>Contact: Daniel Rauh, Technical University of Dortmund, Dortmund, Germany e-mail: daniel.rauh@tu-dortmund.de</p> <p>Contact: Sebastian Bauer, University of Duisburg-Essen Medical School, Essen, Germany e-mail: sebastian.bauer@uk-essen.de</p>