This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Cardiovascular disease				
Hypercholesterolemia	Proprotein convertase subtilisin/kexin type 9 (PCSK9); low-density lipoprotein receptor (LDLR)	<p><i>In vitro</i> studies identified truncated analogs of the epidermal growth factor-like domain A (EGF-A) of LDLR that could aid the design of oral therapeutics to lower cholesterol. PCSK9 binds EGF-A on LDLR, inhibits receptor recycling and thus reduces removal of LDL from the blood. In binding assays, a truncated analog of EGF-A bound PCSK9 with a K_d of $\sim 0.6 \mu\text{M}$ and inhibited its interaction with EGF-A with an IC_{50} of $\sim 18 \mu\text{M}$. In hepatocellular carcinoma cells, the truncated analogs induced LDLR recycling with an EC_{50} of $\sim 25 \mu\text{M}$. This study was performed in collaboration with Pfizer Inc., whose next steps include improving potency and biopharmaceutical properties.</p> <p>Amgen Inc.'s evolocumab, Regeneron Pharmaceuticals Inc. and Sanofi's alirocumab and Pfizer's bococizumab are mAbs targeting PCSK9, and all are in Phase III testing to treat lipid disorders.</p> <p>At least seven additional companies have PCSK9 inhibitors in clinical or preclinical development.</p> <p>SciBX 7(5); doi:10.1038/scibx.2014.143 Published online Feb. 6, 2014</p>	Patent status undisclosed; licensed to Pfizer; unavailable for licensing	<p>Schroeder, C.I. <i>et al. Chem. Biol.</i>; published online Jan. 16, 2014; doi:10.1016/j.chembiol.2013.11.014</p> <p>Contact: David J. Craik, The University of Queensland, Brisbane, Queensland, Australia e-mail: d.craik@imb.uq.edu.au</p>