This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Metabolic disease				
Hypercholesterolemia	Proprotein convertase subtilisin/kexin 9 (PCSK9)	Studies in rodents and nonhuman primates suggest that small interfering RNA against PCSK9, a protease that regulates low-density lipoprotein (LDL) levels, could be useful for treating hypercholesterolemia. In mice and rats, liver-specific siRNA silencing of PCSK9 lowered PCSK9 mRNA levels by 50–70% compared with what was seen using saline buffer control, leading to a 60% decrease in plasma cholesterol concentration. In cynomolgus monkeys, anti-PCSK9 siRNA lowered LDL levels by 50–60% compared with saline buffer control. Next steps include additional preclinical testing of siRNAs targeting PCSK9. Alnylam Pharmaceuticals Inc. has the siRNA-based therapeutic ALN-PCS01 in preclinical development to treat hypercholesterolemia. Isis Pharmaceuticals Inc. and Bristol-Myers Squibb Co. are jointly developing antisense compounds to target PCSK9 compounds for cardiovascular indications.	Series of patents filed for PCSK9 by Alnylam Pharmaceuticals; unlicensed	Frank-Kamenetsky, M. *et al.* *Proc. Natl. Acad. Sci. USA*; published online Aug. 11, 2008; doi:10.1073/pnas.0805434105 **Contact:** Kevin Fitzgerald, Alnylam Pharmaceuticals Inc., Cambridge, Mass. e-mail: kfitzgerald@alnylam.com **Contact:** Cynthia Clayton, same affiliation as above e-mail: cclayton@alnylam.com