This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Neurology				
Schizophrenia	γ-secretase; anterior pharynx defective 1 homologB (Aph1B); neuregulin 1 (Nrg1)	A mouse study suggests that modulating γ-secretase activity could help treat schizophrenia. Aph1B is a subunit of γ-secretase, a protease complex that processes proteins involved in brain development and activity. In mice, Aph1B knockout impaired working memory and sensitivity to both amphetamine and *N*-methyl-D-aspartic acid receptor (NMDAR) agonists compared with what was seen in wild-type controls. Sensitivity to amphetamine implies disturbed dopaminergic signaling, whereas sensitivity to NMDA receptor agonists implies dysregulated glutamatergic signaling. Nrg1, a schizophrenia-linked target of γ-secretase, accumulated in an unprocessed form in Aph1B knockouts but not in wild-type controls. Next steps include testing whether Nrg1 processing can be restored in adults by activating Aph1B and testing whether preclinical γ-secretase modulating compounds can enhance the processing of Nrg1. At least six companies are developing γ-secretase modulators to treat Alzheimer's disease.	Patent pending on use of Aph1B knockout mice as a disease model; available for licensing	Dejaegere, T. *et al. Proc. Natl. Acad. Sci. USA*; published online July 14, 2008; doi:10.1073/pnas.0800507105 **Contact:** Bart De Strooper, University of Leuven, Leuven, Belgium e-mail: bart.destrooper@med.kuleuven.ac.be