This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Neurology				
Alzheimer's disease (AD)	γ -Secretase; presenilin 1 (PSEN1; PS1) PSEN2 (PS2)	<p>A study in mice suggests that AD therapeutics that antagonize γ-secretase could have unwanted side effects on neural activity. In mice, knockout of PS1 and PS2 in presynaptic hippocampal neurons impaired neuronal activity compared with conditional knockout in postsynaptic neurons or no knockout in control mice. PS1 and PS2 are subunits of the γ-secretase complex, which is involved in production of β-amyloid (Aβ) fragments in AD. Next steps include testing the effect of AD-linked mutations in PS1 and PS2 that are implicated in hippocampal function.</p> <p>Eli Lilly and Co. has LY450139, a γ-secretase inhibitor, in Phase III trials for AD. γ-Secretase modulators in Phase I AD testing include Bristol-Myers Squibb Co.'s BMS-299897, Wyeth's GSI-136 and GSI-954, Elan Corp. plc's ELND-006 and Eisai Co. Ltd.'s E2012. γ-Secretase modulators in preclinical development include EnVivo Pharmaceuticals Inc.'s EVP-0962 and Chiesi Farmaceutici S.p.A.'s CHF 5074.</p> <p>SciBX 2(31); doi:10.1038/scibx.2009.1222 Published online Aug. 13, 2009</p>	Patent pending; available for licensing	<p>Zhang, C. <i>et al. Nature</i>; published online July 30, 2009; doi:10.1038/nature08177</p> <p>Contact: Jie Shen, Harvard Medical School, Boston, Mass. e-mail: jshen@rics.bwh.harvard.edu</p> <p>Contact: Chen Zhang, same affiliation as above e-mail: czhang@rics.bwh.harvard.edu</p>