

## This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
<b>Neurology</b>				
Alzheimer's disease (AD)	$\beta$ -site APP-cleaving enzyme 1 (BACE1); $\gamma$ -secretase	<p>A study in cell and mouse tissue culture suggests that raising endosomal pH could help treat AD. In a cell culture model of AD, the generic ion channel blockers bepridil and amiodarone raised endosomal pH, lowered BACE1 and <math>\gamma</math>-secretase activity and reduced production of pathogenic <math>\beta</math>-amyloid (<math>A\beta</math>) compared with no treatment. In brain slices from an AD mouse model, bepridil reduced <math>A\beta</math> to levels comparable to those in vehicle-treated control slices. Next steps include lead optimization to increase <math>\gamma</math>-secretase modulation.</p> <p>Eli Lilly and Co.'s semagacestat (LY450139), a <math>\gamma</math>-secretase inhibitor, is in Phase III testing for AD.</p> <p>Six other companies have preclinical and Phase I compounds that modulate BACE1 and <math>\gamma</math>-secretase to treat AD.</p> <p><b>SciBX 3(28); doi:10.1038/scibx.2010.869</b> Published online July 22, 2010</p>	Unpatented; licensing status not applicable	<p>Mitterreiter, S. <i>et al. J. Neurosci.</i>; published online June 30, 2010; doi:10.1523/JNEUROSCI.1199-10.2010</p> <p><b>Contact:</b> Stefan F. Lichtenthaler, Ludwig Maximilian University of Munich, Munich, Germany e-mail: <a href="mailto:Stefan.lichtenthaler@med.uni-muenchen.de">Stefan.lichtenthaler@med.uni-muenchen.de</a></p>