AbbVie	ABT-089
Mechanism of Action	Nicotinic acetylcholine receptor (nAChR) partial agonist ($\alpha4\beta2$* subtypes) http://www.ncbi.nlm.nih.gov/gene/1137; http://www.ncbi.nlm.nih.gov/gene/1141
Overview	High binding affinity for $\alpha4\beta2$* nAChRs in rat brain (Ki = 17 nM) and human cortex (Ki = 11 nM); lower affinity for $\alpha7$, $\alpha3\beta4$, and muscle nAChRs (Ki > 1000 nM). Partial agonist activity in vitro (<35% the activity of nicotine) but as efficacious as nicotine in increasing glutamate and ACh in rodent cortex in vivo. Active in preclinical cognition assays in rodents and monkeys. Demonstrated efficacy in adults with ADHD in a small Phase 2 proof of concept study, and in a Phase 2, multicenter, randomized, double blind, placebo controlled, dose-ranging study in 221 adults with ADHD, but efficacy endpoints were not met in subsequent phase 2 trials in children with ADHD and in a subsequent trial in adults with ADHD. Efficacy endpoints were not met in a 12-wk phase 2 trial in patients with mild to moderate Alzheimer's disease when ABT-089 was added to cholinesterase inhibitors for 12 weeks.
Safety/Tolerability	Dose-limiting toxicity in rats and dogs characterized by excessive cholinergic stimulation (salivation, emesis, diarrhea, and muscle fasciculations) leading to debilitation and in some cases deaths at high doses. No target organ toxicity was identified in either rat or dog GLP toxicology studies of up to 9 months. In a battery of preclinical safety pharmacology studies, ABT-089 had no significant effect on cardiovascular, pulmonary, or gastrointestinal function, and did not appear to have nicotine-like dependence liability.
Additional Information	Easily absorbed after oral administration in humans. In adults, exhibited linear pharmacokinetics and a half-life of approximately 8 hours. Effect of food on ABT-089 pharmacokinetics was minimal. Primarily eliminated by renal excretion.
Suitable for and Exclusions	Evaluated clinically in both children and adults (including elderly adults). Generally well tolerated in the dose ranges evaluated in ADHD and AD trials, and no marked gender difference at doses administered to both male and female subjects was observed.
Clinical Trials	http://clinicaltrials.gov/ct2/results?term=ABT-089
Publications	http://www.ncbi.nlm.nih.gov/pubmed?term=ABT-089%20or%20ABT089 http://www.ncbi.nlm.nih.gov/pubmed/20203212 http://www.ncbi.nlm.nih.gov/pubmed/19481067 http://www.ncbi.nlm.nih.gov/pubmed/21172907 http://www.ncbi.nlm.nih.gov/pubmed/15179445