Eli Lilly and Company	LY500307
Mechanism of Action	Estrogen receptor β (ERβ, ESR2) agonist/nuclear receptor 3A2 (NR3A2) agonist http://iuphar-db.org/DATABASE/ObjectDisplayForward?objectId=621 http://www.ncbi.nlm.nih.gov/gene/2100
Overview	LY500307 is a small molecule receptor agonist. LY500307 is a potent (EC_{50} 0.66nM) and efficacious (> 5% max) ERb agonist with ~30 fold selectivity over the ERa receptor and > 100 fold selectivity against non-related receptors.
Safety/Tolerability	LY500307 has a weak interaction with hERG (IC_{50} > 1mM). Non-clinical toxicology data supports dosing in man for up-to 24 weeks in duration. The toxicity profile of LY500307 has been characterized in rat, mouse, and monkey. The primary treatment-related findings in rat and monkey repeat-dose toxicity studies up to 6 months in duration were consistent with the estrogenic effects of LY500307.
Additional Information	*In vitro,* LY500307 induces apoptosis in both prostate epithelial and stromal cell lines. In a mouse model, oral administration of LY500307 for 14 days reduced prostate weight (maximum effective dose, ED_{100} 0.1mg/kg/day) without any significant change in circulating testosterone concentrations or seminal vesicle/testes weights. In distribution studies with [^{14}C] LY500307 quantifiable levels of radioactivity were observed in testis, cerebellum, cerebrum, medulla, olfactory lobe, and spinal cord of Long Evans rats, indicating [^{14}C]LY500307-derived radioactivity crossed the blood-testis and blood-brain barriers. LY500307 has completed a Phase 2 multi-center study in men with lower urinary tract symptoms (LUTS) and prostatic enlargement secondary to Benign Prostatic Hyperplasia (BPH). Doses up to 25 mg were well tolerated but without clinical effect.
Suitable for and Exclusions	Role of peripheral and central ERb in human physiology and disease pathophysiology, and biomarker studies for ERb pharmacology. LY500307 is contraindicated in patients who have shown hypersensitivity to any of its components or with known allergies to estrogenic compounds (estrogens/selective estrogen receptor modulators [SERMs]). Patients with known or suspected prostate or breast cancer should not receive LY500307.
Clinical Trials	http://clinicaltrials.gov/ct2/results?term=LY500307
Publications	None