Pfizer Inc.	PF-04191834
Mechanism of Action	5-Lipoxygenase (5-LO) inhibitor http://www.ncbi.nlm.nih.gov/gene/240
Overview	PF-04191834 is a potent (Ki = 10 nM), non-iron chelating, non-redox, selective (~300-fold over 12-LO and 15-LO; no inhibition of the cyclooxygenase enzymes), and competitive inhibitor of the 5-lipoxygenase (5-LO) enzyme.
Safety/Tolerability	In Phase 1 and Phase 2 clinical studies, PF-04191834 was generally safe and well tolerated, except for sporadic, transient, elevations in liver enzymes, occasionally to the level of clinical concern, including one serious adverse event of potential drug-induced liver injury. As other 5-LO inhibitors (both redox and non-redox mode of action) have been linked to hepatic toxicity in humans, this may be a pharmacology class-related effect. Nonclinical toxicology data support clinical studies up to 6 weeks in duration.
Additional Information	In clinical studies, PF-04194834 at 300 or 600 mg BID for 7 days achieved ≥ 90% suppression of urinary leukotriene E4 (LTE4) excretion, a biomarker of systemic 5-LO inhibition. PF-04191834 appeared to demonstrate pharmacodynamic activity (acute bronchodilatation at 12 hours) after single doses in mild asthmatics. It failed to demonstrate efficacy in a 2-week study in knee osteoarthritis pain.
Suitable for and Exclusions	Benefit/risk is most plausible in acute, sub-acute and/or high morbidity indications given the potential for drug-induced liver injury.
Clinical Trials	http://www.clinicaltrials.gov/search?term=%22PF-04191834%22
Publications	http://jpet.aspetjournals.org/content/334/1/294.full.pdf+html