Janssen Research & Development, LLC	JNJ-18038683
Mechanism of Action	5-Hydroxytryptamine 7 receptor (5-HT7) antagonist http://iuphar-db.org/DATABASE/ObjectDisplayForward?objectId=12 http://www.ncbi.nlm.nih.gov/gene/3363
Overview	JNJ-18038683 is a high affinity relatively selective 5-HT7 receptor antagonist. After oral administration, JNJ-18038683 dose-dependently increased rapid eye movement (REM) sleep latency and decreased the amount of REM sleep in rats, mimicking the effect of most antidepressants on sleep architecture. JNJ-18038683 also potentiated the increase of REM latency and the REM sleep decrease induced by citalopram. JNJ-18038683 dose-dependently decreased immobility time in the mouse tail suspension test, a preclinical model of antidepressant activity. In addition, JNJ-18038683 enhanced citalopram-induced antidepressant-like effects in the mouse tail suspension test. JNJ-18038683 has a full package of GLP preclinical studies, including cardiovascular safety and genotoxicity, and has entered phase 2a.
Safety/Tolerability	Good Laboratory Practice toxicological studies were conducted in rat and dog and indicated that JNJ-18038683 has a suitable safety profile to allow testing in humans. JNJ-18038683 was well tolerated in single and multiple dose studies of up to 13 weeks duration. In both rats and dogs, the primary toxicities were neurologic (ptosis and clinical signs of sedation) or gastrointestinal (decreased food consumption, salivation, emesis, fecal changes). In standard tests to assess embryo-fetal safety, genotoxicity, and phototoxicity potential, JNJ-18038683 was also shown to be well tolerated. During the single and multiple ascending-dose studies, no serious adverse events were reported and most adverse events were mild indicating that JNJ-18038683 is well tolerated in healthy volunteers.
Additional Information	In healthy human volunteers, JNJ-18038683 prolonged REM latency and reduced REM sleep duration demonstrating target engagement. JNJ-18038683 enhanced REM sleep suppression induced by citalopram in humans, although a drug-drug interaction could not be ruled out. In a double blind, active- and placebo-controlled clinical trial in 225 patients suffering from major depressive disorder, neither treatment with pharmacologically active doses of JNJ-18038683 or escitalopram separated from placebo indicating a failed study lacking assay sensitivity.
Suitable for and Exclusions	Major depressive disorder, migraine.
Clinical Trials	http://clinicaltrials.gov/ct2/results?term=JNJ-18038683
Publications	http://www.cinpasia.com/abstract/51.asp http://www.ncbi.nlm.nih.gov/pubmed?term=JNJ-18038683