

Pfizer Inc.	SD-7300 (SC-81490)
Mechanism of Action	Matrix metalloproteinase (MMP) 2, 9, and 13 inhibitor http://www.ncbi.nlm.nih.gov/gene/4313 ; http://www.ncbi.nlm.nih.gov/gene/4318 ; http://www.ncbi.nlm.nih.gov/gene/4322
Overview	SD-7300 is a potent ($K_i = 0.03, 0.01$ and 0.03 nM for MMP-2, 9, and 13, respectively), selective [$(K_i = 2070, 1.4, 3040, 0.4, 28$ and 790 nM for MMP-1, 3, 7, 8, 14, and TNFalpha converting enzyme (TACE), respectively)], reversible inhibitor of human MMP-2, 9, and 13. Potency on rat MMP-13 is ~10-fold less.
Safety/Tolerability	SD-7300 was generally safe and well tolerated in normal volunteers in single and multiple doses (up to seven days) ranging from 25 to 1200 mg BID. At doses > 200 mg BID, dose-dependent prolongation of the QTc interval was detected. Ketoconazole increases exposure. Nonclinical toxicology data support clinical studies up to at least 4, and possibly 13, weeks in duration. SD-7300 was teratogenic in embryofetal toxicology studies.
Additional Information	Pharmacodynamic evidence of target coverage was demonstrated in humans by decrease in urinary collagen breakdown fragments; projected human dose for efficacy is ≥ 15 mg BID (or 75 mg QD). Nonclinical studies with SD-7300, and clinical experience with other drugs in this class, suggest the possibility of a reversible musculoskeletal syndrome (MSS) with chronic (> 4 weeks) dosing. Cataract formation was also noted in nonclinical studies dosed for > 4 weeks.
Suitable for and Exclusions	Clinical studies up to 4 weeks in duration with close monitoring (particularly for cardiac arrhythmias, QTc prolongation, and cataract formation) at doses < 200 mg BID. Women of childbearing potential should be excluded. Concomitant administration of drugs that prolong QTc interval or that are moderate to strong CYP3A4 inhibitors/inducers are contraindicated.
Clinical Trials	Only Phase 1 (see above) to date
Publications	http://pubs.acs.org/doi/pdfplus/10.1021/jm100669j http://www.sciencedirect.com/science/article/pii/S0003269706007780