ACS Medicinal Chemistry Letters

PATENT HIGHLIGHT

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Quinoline Derivatives as 5-HT$_6$ Receptor PET Ligands

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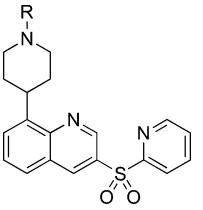
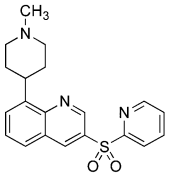
Title:	Quinoline Derivatives as 5-HT$_6$ Receptor PET Ligands		
Patent/Patent Application Number:	US-20130343993-A1	**Publication date:**	December 26, 2013
Priority Application:	US-20130343993-A1	**Priority date:**	January 08, 2012
Inventors:	Black, L. A.		
Assignee Company:	AbbVie Inc. USA		
Disease Area:	Alzheimer's Disease, deficits in memory, cognition, and learning	**Biological Target:**	5-HT$_6$ receptor

Summary: This application claims a series of quinolines for treating or preventing a condition or disorder related to memory deficits such as Parkinson's disease, Alzheimer's disease, mild cognitive impairment, depression, and anxiety. The invention claims also radiolabeled quinolines useful as diagnostic tools as 5-HT$_6$ receptor PET ligands.

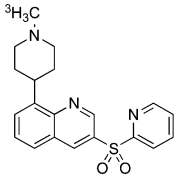
Important Compound Classes:



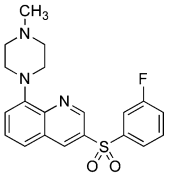
Key Structures:



Example 1



Example 2



GSK-215083

Biological Assay: Compounds were evaluated in 5-HT$_6$, 5-HT$_{2A}$, and 5-HT$_{2B}$ receptor binding assays and against a panel of 78 receptors/drug targets.

Biological Data:

Compounds binding affinities

	Example 1	GSK-215083
Human 5-HT$_6$ K$_i$ (nM)	0.22	0.34
Human 5-HT$_{2A}$ K$_i$ (nM)	123 (559x)	0.39 (1.16x)
Human 5-HT$_{2B}$ K$_i$ (nM)	144 (654x)	

Rat PK (0.05 mg/kg, iv) for Example 1

Minutes after dose	Plasma conc. (ng/mL)	Free brain conc. (ng/g)	Free B/P ratio
3	104.5	21.5	0.21
5	83.5	23.1	0.28

Brain Distribution for Tritium Labeled Example 2

Minutes after dose	Stratium/ Cer.	Hippocampus/ Cer.	Cortex/Cer.
5	0.81	1.06	0.9
40	1.31	1.07	1.20

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Notes
The authors declare no competing financial interest.