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Imidazotriazinone Compounds

Patent Highlight

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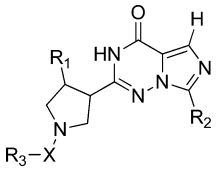
Title:	Imidazotriazinone Compounds		
Patent Application Number:	WO 2012/040230	**Publication Date:**	March 29, 2012
Priority Application:	61/384694	**Priority Date:**	September 20, 2010
Inventors:	Ripka, A.; Shapiro, G.; McRiner, A.		
Assignee Company:	EnVivo Pharmaceuticals		
Disease Area:	Neurodegenerative Disease	**Biological Target:**	PDE9

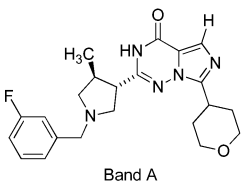
Summary: This application claims a series of imidazotriazinone PDE9 inhibitors. PDE9 is a cGMP-selective phosphodiesterase that is implicated as a potential target in a range of CNS diseases including Alzheimer's Disease and other cognitive disorders.

Primary Markush:

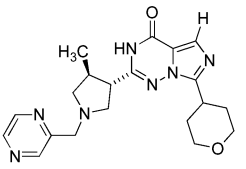


Definitions: X = bond, carbonyl, or SO_2, R_1 = H, alkyl, cycloalkyl, heterocycloalkyl including substituted derivatives, R_2 = cycloalkyl, heterocycloalkyl, phenyl, heteroaryl including substituted derivatives, R_3 = alkyl, cycloalkyl, heterocycloalkyl including substituted derivatives.

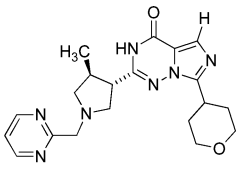
Notable Substructures:



Band A
> 1000-fold selectivity



Band B
selectivity not determined



Band C
selectivity not determined

Biological Assay: PDE assays were conducted using a Caliper LabChip instrument, and enzyme activity was measured spectrophotometrically to detect hydrolysis of a fluorescently labeled cyclic nucleotide. Selectivity against all other PDEs was measured. The patent reports fold selectivity versus PDE1A and PDE1B.

Biological Data: PDE inhibition data was provided by banding compounds: band A, IC50 < 1 μM; band B, 1−10 μM; band C, >10 μM.

Additional Information PDE9 inhibitors are attracting attention for treatment of CNS disorders that can be influenced by elevation in cGMP levels. A PDE9 inhibitor, PF-04447943, is currently in clinical trials for cognitive disorders. The genus claimed in this application is reminiscent of the core structure of vardenafil, a PDE5 inhibitor related to sildenafil.

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Notes

The authors declare no competing financial interest.

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