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PATENT HIGHLIGHT

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Novel Pyridyloxadiazole Agonists of Sphingosin-1-phosphate

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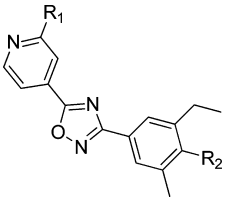
Title:	Novel Pyridyloxadiazole Agonists of Sphingosin-1-phosphate		
Patent/Patent Application Number:	WO 2014/141171 A1	**Publication date:**	September 18, 2014
Priority Application:	EP 2013-159482	**Priority date:**	March 15, 2013
Inventors:	Bolli, M.; Lescop, C.; Nayler, O.; Steiner, B.		
Assignee Company:	Actelion Pharmaceuticals, Ltd., Switzerland		
Disease Area:	Autoimmune system disorders	**Biological Target:**	Sphingosin-1-phosphate 1 receptor ($S1P_1$)

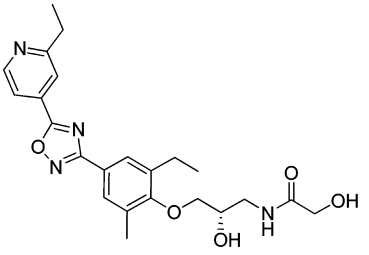
Summary: The present application discloses a series of pyridyloxadiazoles as agonists of $S1P_1$. The compounds of the invention show a certain level of selectivity for $S1P_1$ receptor over the $S1P_3$ receptor. The compounds claimed here are potentially useful in the treatment of a wide range of disorders such as rejection of transplanted organs, rheumatoid arthritis, multiple sclerosis, Crohn's disease, psoriasis, asthma, type I diabetes, and cancer.

FYK720, Gilenya, an agonist of S1P1, S1P3, S1P4, and S1P5 receptors, is the first orally bioavailable drug approved for the treatment of multiple sclerosis.

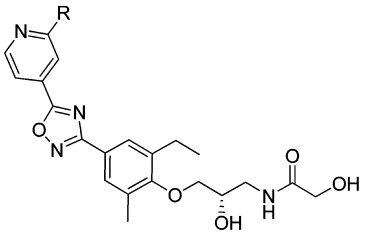
Important Compound Classes:



Key Structures:



Compound 1



Compound	R	Compound	R
2	n-propyl	**6**	isopentyl
3	isopropyl	**7**	pentyl-3-yl
4	n-butyl	**8**	cyclopentyl
5	isobutyl		

Biological Assay: The agonistic activity of the compounds was evaluated using a GTPγS binding assay in CHO cells expressing recombinant human $S1P_1$ receptor or $S1P_3$ receptor.

Pharmacological Data:

Compound	$S1P_1$ EC_{50} (nM)	$S1P_3$ EC_{50} (nM)
1	2.1	9950
2	0.7	1120
3	0.3	3940
4	1.8	700
5	0.2	757
6	5.1	2600
7	0.1	1340
8	0.1	736

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Notes
The authors declare no competing financial interest.