ACS Medicinal Chemistry Letters

PATENT HIGHLIGHT

pubs.acs.org/acsmedchemlett

Pyrazolsulfonamide Agonists of Oxytocin Receptor

Gerard Rosse*

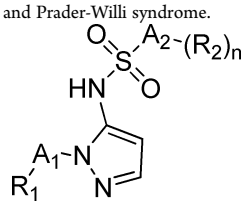
Structure Guided Chemistry, Dart Neuroscience LLC, 7473 Lusk Boulevard, San Diego, California 92121, United States

Adjunct Associate Professor, Department of Pharmacology and Physiology, College of Medicine, Drexel University, New College Building, 245 North 15th Street, Philadelphia, Pennsylvania 19102, United States

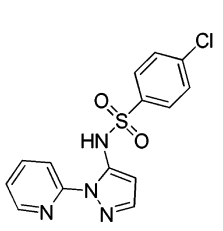
Title:	Pyrazolsulfonamide Agonists of Oxytocin Receptor		
Patent/Patent Application Number:	WO 2014/111356 A1	**Publication date:**	July 24, 2014
Priority Application:	EP 2013-151632	**Priority date:**	January 17, 2013
Inventors:	Bissantz, C.; Grundschober, C.; Nettekoven, M.; Plancher, J.-M.; Vifian, W.		
Assignee Company:	Hoffmann-La Roche, Inc.		
Disease Area:	CNS	**Biological Target:**	Oxytocin receptor

Summary: The present application discloses a series of pyrazolsulfonamides as agonists of the oxytocin receptor. Oxytocin is a nine amino acid cyclic peptide hormone; it is a potent uterotonic agent clinically used to induce labor. Oxytocin and its receptors exist in the nucleus accumbens and the hippocampus. Agonists of the oxytocin receptor are claimed as potential treatment for a variety of CNS diseases such as autism, schizophrenia, anxiety disorders, drug addiction, and Prader-Willi syndrome.

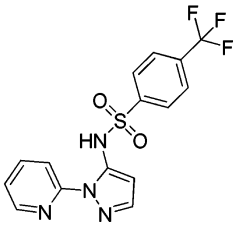
Important Compound Classes:



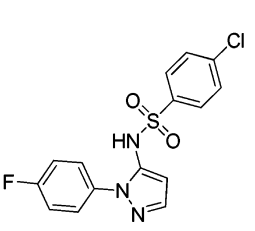
Key Structures:



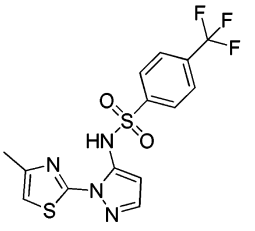
Compound 1



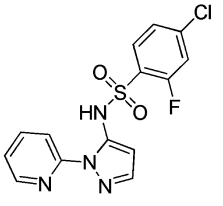
Compound 2



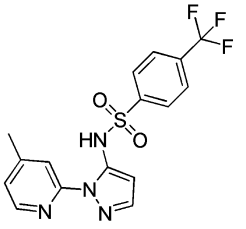
Compound 7



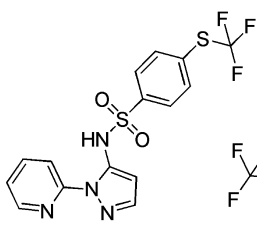
Compound 9



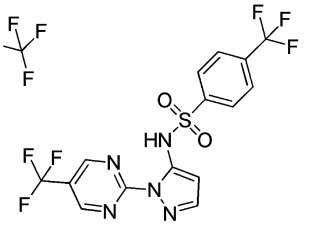
Compound 14



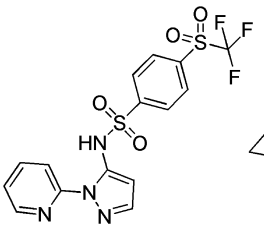
Compound 16



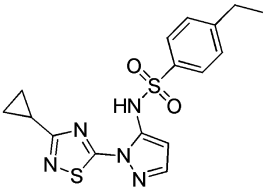
Compound 20



Compound 21



Compound 23



Compound 25

Received: October 25, 2014
Published: October 31, 2014

dx.doi.org/10.1021/ml5004348 | *ACS Med. Chem. Lett.* 2014, 5, 1188–1189

Recent Review Articles: Yamasue H. Function and structure in social brain regions can link oxytocin-receptor genes with autistic social behavior. *Brain Dev.* **2013**, *35* (2), 111−118.

Biological Assay: A calcium flux assay using fluorescence imaging (FLIPR) was developed to evaluate compounds efficacy.

Pharmacological Data:

Compound	hEC_{50} (μM)	Compound	hEC_{50} (μM)
1	0.019	**16**	0.017
2	0.008	**20**	0.047
7	2.460	**21**	1.570
9	0.520	**23**	0.753
14	0.019	**25**	1.570

Synthesis: The synthesis of 26 compounds is described.

AUTHOR INFORMATION

Corresponding Author

*E-mail: grosse@dartneuroscience.com.

Notes

The authors declare no competing financial interest.