ACS Medicinal Chemistry Letters

PATENT HIGHLIGHT

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# Triazolo Derivatives as Inhibitors of PDE10A

Jean-Francois Brazeau[†] and 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:** Triazolo Derivatives as Inhibitors of PDE10A

**Patent/Patent Application Number:** WO 2013/178512 A1 **Publication Date:** December 5, 2013

**Priority Application:** EP 2012-1696954 **Priority Date:** May 30, 2012

**Inventors:** Flohr, A.; Groebke Zbinden, K.; Kuhn, B.; Lerner, C.; Rudolph, M.; Schaffhauser, H.

**Assignee Company:** Hoffmann-La Roche Inc.

**Disease Area:** CNS **Biological Target:** PDE10A

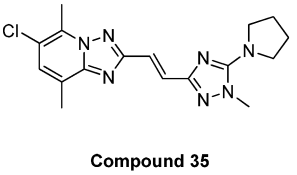
**Summary:**

The present application discloses a series of triazolo analogues capable of inhibiting the activity of PDE10A, a unique enzyme from the phosphodiesterase family. It is suggested that this enzyme plays a key role in various physiological functions and diseases that can be treated by PDE10A inhibitors including, but not limited to, certain psychotic and neurodegenerative disorders such as schizophrenia, acute stress disorder, drug addictions, obsessive/compulsive disorders, movement disorders, cognition deficiency disorders, and bipolar disorders.

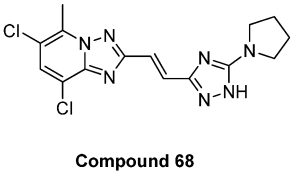
**Important Compound Classes:**

B is C1-C4-alkylene, C2-C4-alkenylene, C2-C4-alkynylene, C3-C5-cycloalkyl

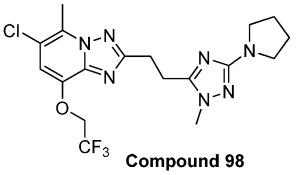
**Key Structures:**



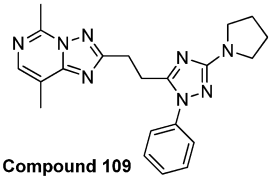
Compound 35



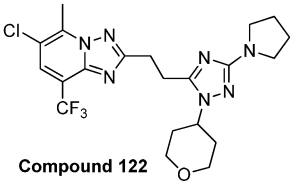
Compound 68



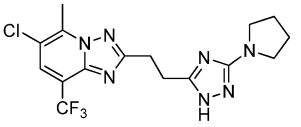
Compound 98



Compound 109



Compound 122



Compound 128

**Recent Review Articles:** Menniti, F. S.; Chappie, T. A.; Humphrey, J. M.; Schmidt, C. J. *Curr. Opin. Invest. Drugs* **2007**, *8*, 54−59.

**Biological Assay:** Compound efficacy was evaluated using cAMP binding assay.

**Pharmacological Data:**

| | $IC_{50}$ (nM) |
|---|---|
| Compound **35** | 0.15 |
| Compound **68** | 0.22 |
| Compound **98** | 0.51 |
| Compound **109** | 0.29 |
| Compound **122** | 0.25 |
| Compound **128** | 0.72 |

**Synthesis:** 136 compounds were synthesized

## AUTHOR INFORMATION

### Corresponding Author

*E-mail: grosse@dartneuroscience.com.

### Notes

The authors declare no competing financial interest.

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