ACS Medicinal Chemistry Letters

PATENT HIGHLIGHT

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Novel Benzoisoxazoloazepine Inhibitors of Bromodomain-Containing Proteins

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Title: Novel Benzoisoxazoloazepine Inhibitors of Bromodomain-Containing Proteins

Patent/Patent Application Number: WO 2013/184876 A1 **Publication Date:** December 12, 2013

Priority Application: US 2012-61656205 **Priority Date:** June 6, 2012

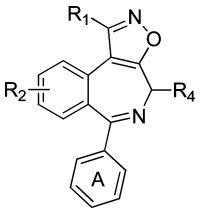
Inventors: Albrecht, B. K.; Hewitt, M. C.; Gehling, V. S.; Vaswani R. G.

Assignee Company: Constellation Pharmaceuticals, Inc., USA

Disease Area: Cancer **Biological Target:** Bromodomain-containing proteins, BRD4

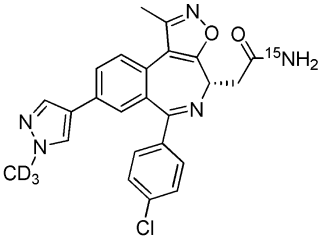
Summary: The present application claims a series of benzoisoxazoloazepine to serve as inhibitors of bromodomain-containing proteins. The compounds described in this patent application could potentially be useful for the treatment of cancer, inflammatory disease, autoimmune disease, or viral infection.

Important Compound Classes:

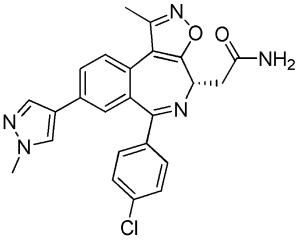


Definitions: Phenyl ring A is optionally substituted

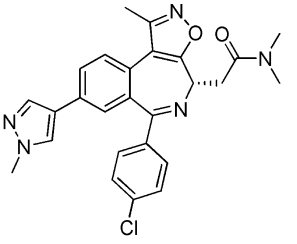
Key Structures:



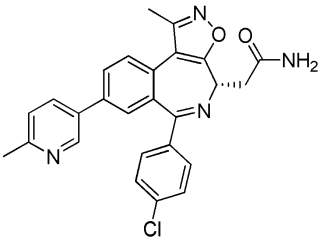
Compound 400



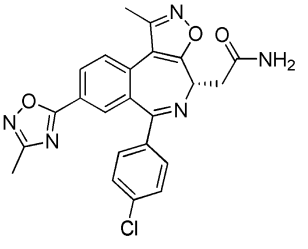
Compound 401



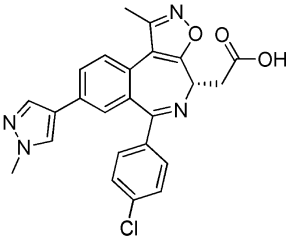
Compound 402



Compound 403



Compound 404



Compound 405

Recent Review Articles: Gallenkamp, D.; Gelato, K. A.; Haendler, B.Weinman, H. Bromodomains and Their Pharmacological Inhibitors, *ChemMedChem* **2014**, *9* (3), 438−464.

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Biological Assay: A BRD4 AlphaLisa assay was used to evaluate the binding of H4-tetraacetylated histone and BRD4.

Pharmacological Data:

	Alphascreen Assay (IC_{50}, nM)
Compound **400**	18
Compound **401**	14
Compound **402**	13
Compound **403**	28
Compound **404**	270
Compound **405**	175

Synthesis: The synthesis of 405 compounds is described.

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Notes

The authors declare no competing financial interest.