ACS Medicinal Chemistry Letters

PATENT HIGHLIGHT

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Triazolo[4,5-d]pyrimidine Derivatives as Inhibitors of GCN2

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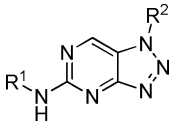
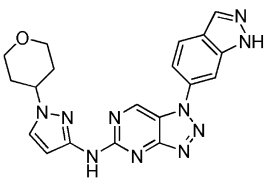
Title:	Triazolo[4,5-d]pyrimidine Derivatives as Inhibitors of GCN2		
Patent/Patent Application Number:	WO 2013110309	**Publication date:**	August 1, 2013
Priority Application:	EP 2012-558	**Priority date:**	January 28, 2012
Inventors:	Dorsch, D.; Hoelzemann, G.; Schiemann, K.; Wagener, A.		
Assignee Company:	Merck GMBH, Germany		
Disease Area:	Cancer	**Biological Target:**	GCN2 protein kinase

Summary: The present application claims a series of triazolopyrimidine analogues that inhibit the stress response of general control nonderepressible 2 kinase (GCN2) and that may be useful as chemotherapeutic drugs for the treatment of cancer.

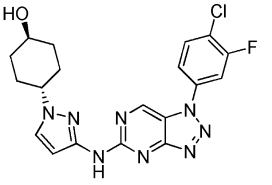
Important Compound Classes:



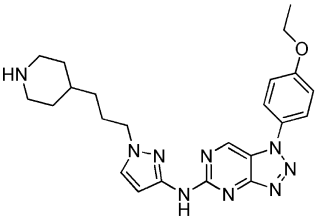
Key Structures:



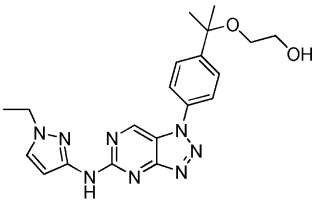
Compound A-92



Compound A-103



Compound A-125



Compound A-127

Recent Review Articles: Ye, J.; Kumanova, M.; Hart, L. S.; Sloane, K.; Zhang, H.; De Panis, D. N.; Bobrovnikova-Marjon, E.; Diehl, J. A.; Ron, D.; Koumenis, C. *EMBO J.* **2010**, *29*, 2082.

Biological Assay: The enzyme assay was developed using serine kinase GCN2, and the cellular assay was developed using the primary antibody (antiphospho-elF2alpha)

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Pharmacological Data:

	IC_{50} GCN2 (Enzyme Assay)	IC_{50} GCN2 (Cell Assay)
Compound **A-92**	<0.3 μM	<0.3 μM
Compound **A-103**	<0.3 μM	<0.3 μM
Compound **A-125**	<0.3 μM	<0.3 μM
Compound **A-127**	<0.3 μM	0.3 - 3 μM

Synthesis: (optional) 157 compounds were prepared.

AUTHOR INFORMATION

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Notes
The authors declare no competing financial interest.