ACS Medicinal Chemistry Letters

PATENT HIGHLIGHT

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Pyrrolopyridines-quinazolines Inhibitors of PKR-Like ER Kinase

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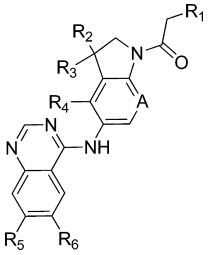
Title:	Pyrrolopyridines-quinazolines Inhibitors of PKR-Like ER Kinase		
Patent/Patent Application Number:	WO 2014/161808 A1	**Publication date:**	October 9, 2014
Priority Application:	EP 2013−162362	**Priority date:**	April 4, 2013
Inventors:	Stansfield, I.; Ligny, Y. A. E.; Amblard, N. C., I.; Versele, M. L. A.		
Assignee Company:	Janssen Pharmaceutica NV, Belgium		
Disease Area:	Cancer, diabetes, and neurodegenerative diseases	**Biological Target:**	PKR-like ER kinase (PERK)

Summary: The present application claims pyrrolopyridines-quinazolines analogues as inhibitors of PERK kinase. The compounds of the invention are potentially useful in the treatment of a wide range of disorders such as cancer, diabetes, ocular disease, stroke, inflammation, viral infections, and neurodegenerative diseases.

Important Compound Classes:

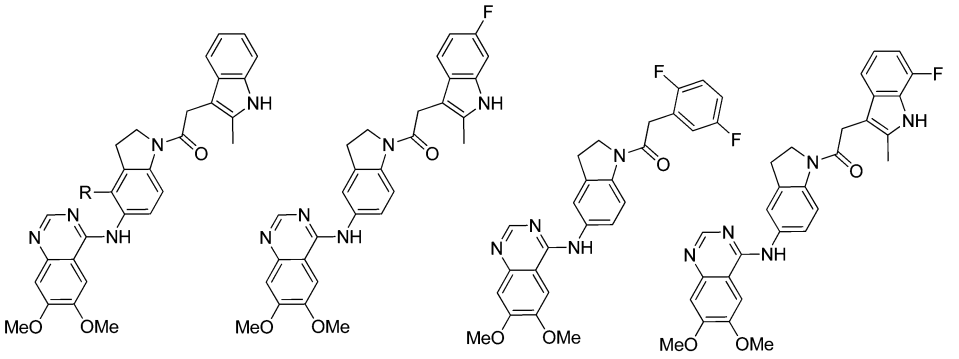


Definitions: A = CH or N

Special Issue: New Frontiers in Kinases

Received: November 24, 2014
Published: December 08, 2014

Key Structures:

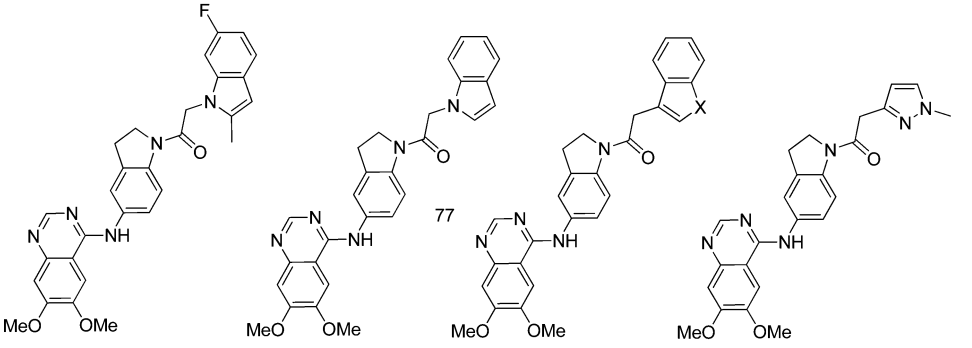


Compound 1, R=H
Compound 39, R=F

Compound 2

Compound 3

Compound 4



Compound 7

Compound 15

Compound 16, X=NH
Compound 30, X=O

Compound 28

Biological Assay: The enzymatic activity of the compounds was evaluated in a PERK kinase assay using LanthaScreen technology and in a cell-based TR-FRET assay in HEK293 cells.

Pharmacological Data:

Enzymatic assays

Compound	PERK pIC_{50}	Cell PERK pIC_{50}
1	9.1	7.7
2	9.2	7.6
3	9.4	7.3
4	8.8	7.4
7	8.5	7.1
15	8.2	6.5
16	8.3	6.3
28	6.6	5.1
30	8.0	<4.5
39	9.0	7.9

Synthesis: The synthesis of 153 compounds is described.

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Notes
The authors declare no competing financial interest.