ACS Medicinal Chemistry Letters

PATENT HIGHLIGHT

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Combination of Novel Imidazopyridazine Mps-1 Kinase Inhibitors and Bcl-2 Family Protein Inhibitors

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Title: Combination of Novel Imidazopyridazine Mps-1 Kinase Inhibitors and Bcl-2 Family Protein Inhibitors

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Priority Application: EP 2012-178985 **Priority Date:** August, 2, 2012

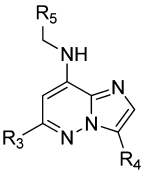
Inventors: Siemeister, G.; Bader, B.; Wengner, A. M.; Mumberg, D.; Koppitz, M.; Klar, U.; Kroemer, G.; Vitale, I.; Jemaa, M.

Assignee Company: BAYER Pharma AG, Germany

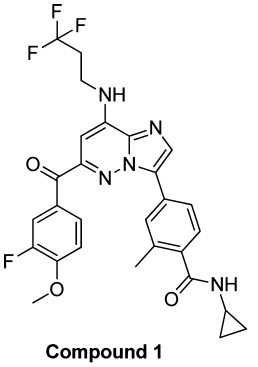
Disease Area: Cancer **Biological Target:** Monopolar spindle 1 kinase (Mps-1) and antiapoptotic protein of the Bcl-2 family

Summary: The present application describes imidazopyridazine derivatives (compound A) in combination with an inhibitor of an antiapoptotic protein of the Bcl-2 family (compound B) for the treatment of cancer. Compound B is selected from a group consisting of Obatoclax, Navitoclax, Beclanorsen, VMD-8018, Oblimersen, Apogossypol, 1133719, PNT-100, HG-1113, S-44563, ABT-731, ONY-701, BP-100-1.02, and AT-101. The combination described in this patent application could potentially be useful for the treatment of lung, melanoma, pancreatic, and breast cancer.

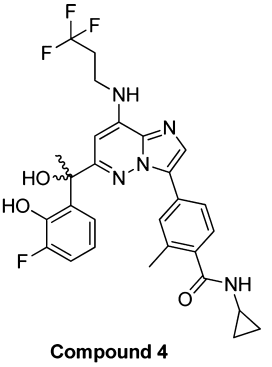
Important Compound Classes:



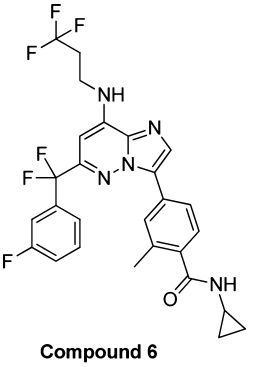
Key Structures:



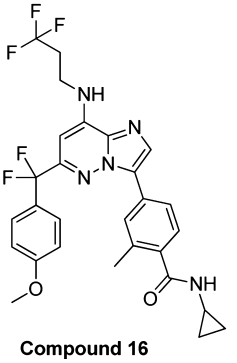
Compound 1



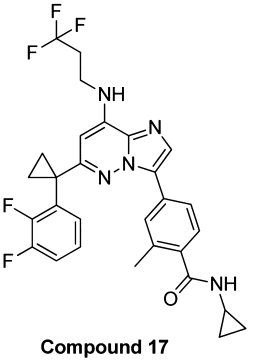
Compound 4



Compound 6



Compound 16



Compound 17

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Biological Assay: The inhibition of the Mps-1 kinase activity was evaluated using a TR-FRET assay.

Pharmacological Data:

	Mps-1 (IC_{50}, nM)
Compound **1**	0.4
Compound **4**	0.3
Compound **6**	0.7
Compound **16**	0.6
Compound **17**	0.7

Synthesis: (optional) The synthesis of 32 compounds is described.

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Notes
The authors declare no competing financial interest.