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Patent Highlight

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Novel Amino-Nicotinamide Derivatives as Modulators of KCNQ2/3 Potassium Channels

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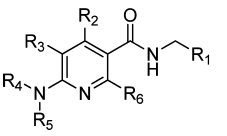
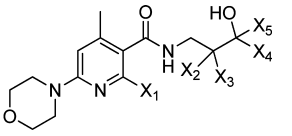
Title:	Novel Amino-Nicotinamide Derivatives as Modulators of KCNQ2/3 Potassium Channels		
Patent/Patent Application Number:	US 2012/0258947 A1	**Publication Date:**	October 11, 2012
Priority Application:	EP 2010-13811	**Priority Date:**	October 10, 2010
	US 2010-394868P		October 20, 2010
	US 2011-276464		October 19, 2011
Inventors:	Kuhnert, S.; Bahrenberg, G.; Kless, A.; Schroder, W.; Lucas, S.		
Assignee Company:	Grunenthal GmbH, Germany		
Disease Area:	pain, anxiety, epilepsy, cognitive diseases	**Biological Target:**	KCNQ2/3 potassium channels

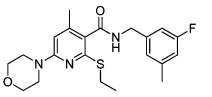
Summary: This invention provides a novel series of amino-nicotinamides which modulates the function of KCNQ2/3 potassium channels for the treatment and/or prophylaxis of pain.

Important Compound Classes:

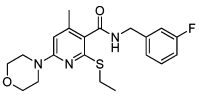




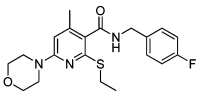
Key Structures:



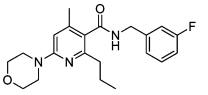
Example 1



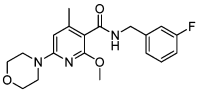
Example 2



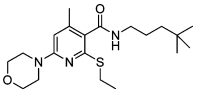
Example 4



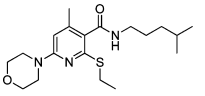
Example 10



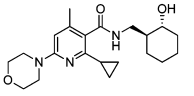
Example 19



Example 67



Example 79



Example X2

Biological Assays (Description): Compound potency was measured in a fluorescence assay using human CHO-K-1 cell expressing KCNQ2/3 channels. Antinociceptive effect of the compounds was evaluated in the low intensity tail flick test in rat.

Pharmacological Data:

Example	Fluorimetry % efficacy (retigabine = 100%)	Fluorimetry EC_{50}/IC_{50} [nM]	Low intensity tail flick, rat, peroral, ED_{50} or MPE (dose) [mg/kg]
1	160	56	78 (4.64)
2	171	134	4.3
4	158	124	94 (10)
10	176	181	81 (10)
19	155	736	79 (10)
67	244	42	100 (10)
79	215	206	46 (10)
X2	245	483	67 (10)

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Synthesis:	Synthesis of 362 compounds
Claims:	Claim 30: Use of the compound for the treatment of pain, epilepsy anxiety, bipolar disorders, and cognitive disease.

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Notes

The author declares no competing financial interest.