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Viewpoint

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Potassium Channel Modulators as Possible Treatment for Pain

Patent Highlight

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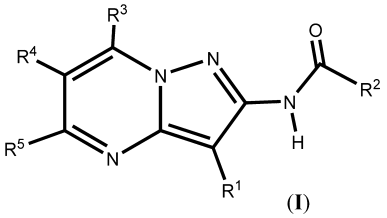
Title:	Pyrazolo[1,5-*a*]pyrimidin Potassium Channel Modulators		
Patent/Patent Application Number:	WO/2012/067822A1	**Publication Date:**	May 24, 2012
Priority Application:	61/414,275	**Priority Date:**	November 16, 2010, US
Inventors:	Xu, Xiandong; Van Camp, Jennifer; Scanio, Marc J.; Bunnelle, William H.; Shi, Lei; Osuma, Augustine T.; Degoey, David; Perez-Medrano, Arturo; Peddi, Sridhar; Patel, Jyoti R.		
Assignee Company:	Abbott Laboratories, 100 Abbott Park Road, Abbott Park, Illinois 60064, United States		
Disease Area:	Pain	**Biological Target:**	KCNQ Potassium Channels

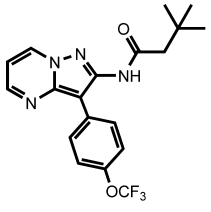
Summary: The compounds of Formula (**I**) are KCNQ potassium channel modulators (openers) and are claimed for treatment of pain. KCNQ (aka Kv7) represents a family of membrane-bound proteins responsible for regulating the flow of potassium ions through cell membranes. Studies have shown that activation of KCNQ by KCNQ modulators (openers) results in the outflow of K^+ ions from the cell, thus reducing the membrane potential (a process known as hyperpolarization), thus controlling cellular excitability. This activity by KCNQ openers can potentially treat several CNS disorders characterized by neuronal hyperexcitability, such as migraine, epilepsy, and neuropathic pain, as well as anxiety and overactive bladder. While the patent lists several potential uses, the treatment of pain is the only claimed use.

Important Compound Classes: The structures claimed in the application are represented generally by formula (I):

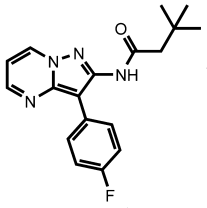


(**I**)

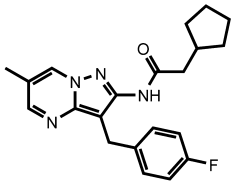
Key Structures: The patent application described the synthesis of 185 examples, all claimed specifically by name. The following are three of the listed examples:



Example 1



Example 2



Example 5

Biological Data: The in vitro EC_{50} values for most of the 185 examples are tabulated to identify compounds that activate KCNQ 2 and 3 channels; the EC_{50}values for the first six examples are shown in the following table:

Example No.	EC_{50}	Definitions
Example 1	C	**A** represents EC_{50} of < 100 nM **B** represents EC_{50} between 100 nM to < 500 nM **C** represents EC_{50} between 500 nM to < 1000 nM **D** represents EC_{50} between 1000 nM to < 10,000 nM **E** represents EC_{50} of about and > 10,000 nM
Example 2	D	
Example 3	B	
Example 4	C	
Example 5	A	
Example 7	B	

Claims: Claims 1−23: composition of matter; variations of formula (I)

Claim 24: 146 examples of the compounds of formula (I) are claimed specifically by name

Claim 25: a pharmaceutical composition

Claim 26: a method for treating pain

Published: July 10, 2012

dx.doi.org/10.1021/ml300154z | *ACS Med. Chem. Lett.* 2012, 3, 608−609

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Notes

The authors declare no competing financial interest.