



Central Nervous System Pain Program

DECEMBER 2009

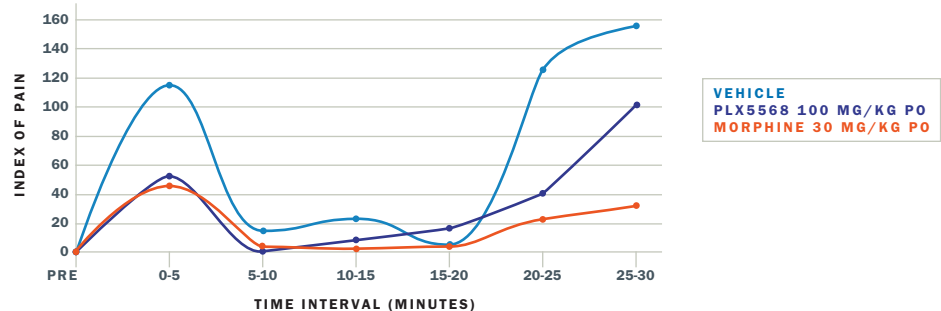
→ PLX5568

Plexxikon's lead program in pain is a novel small molecule kinase inhibitor—and an orally active, non-opioid agent with opiate-like efficacy. The compound has demonstrated attractive pharmaceutical properties and in vivo efficacy in multiple models of pain. In preclinical models, Plexxikon's development candidate appears effective in treating acute, inflammatory and neuropathic pain.

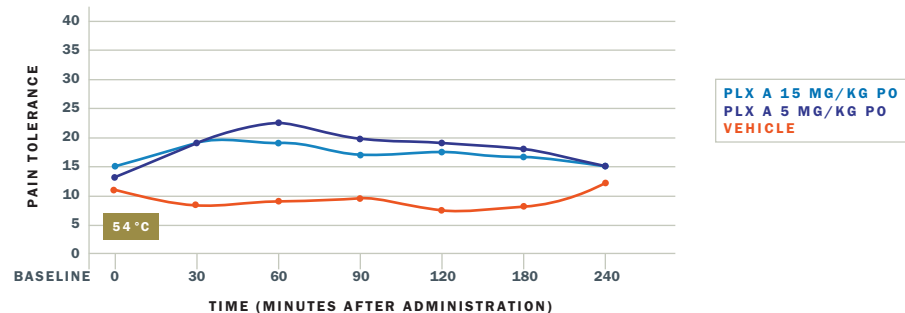
A number of kinase targets are critical modulators of neurotransmitter signals that determine nociception. Therefore, kinase inhibition offers a novel mechanism of analgesia that should differentiate effectively from current NSAIDs and opioids with similar levels of pain relief.

→ Novel Non-Opioid Agent Demonstrates Opiate-like Efficacy

Plexxikon's development candidate has demonstrated in vivo efficacy in multiple models of pain. This compound has shown efficacy equivalent to morphine, even at low doses.



PLEXXIKON COMPOUND REDUCES PAIN IN BOTH ACUTE AND INFLAMMATORY PHASES



POTENT ANALGESIC EFFECT DEMONSTRATED EVEN AT LOW DOSES

Program Highlights

- Status: Phase 1 ongoing
- Unpartnered

→ Highly Selective Kinase Inhibitors Can Address Huge Unmet Needs Outside Oncology

Plexxikon's platform has proven particularly amenable to the development of highly selective, dual or pan modulators, including very selective kinase inhibitors. For a large and significant drug target family such as kinases, designing selective drug candidates provides new and promising treatments in a variety of indications—even outside oncology indications—where safety hurdles can be much higher. PLX5568 has been tested across a wide panel of kinases and is highly selective for a single kinase target.

PLX5568	SELECTIVITY
195 KINASES	>1000-FOLD*
19 KINASES	>100-FOLD
5 KINASES	>10-FOLD
1 KINASE	~8-FOLD
TARGET KINASE	

HIGHLY SELECTIVE KINASE INHIBITOR
*includes kinases < 20% inhibition at 1 μ M

→ Phase I Candidate for Significant Market Opportunity

While pain management products currently represent a multi-billion market, there is still a significant unmet medical need in the moderately severe and severe segments of this market. Plexxikon's oral, non-opioid agent with an acute onset of action and opiate-like efficacy could expand this segment further. Additionally, this market is expected to increase greatly as the overall population ages.

Plexxikon is conducting a Phase 1 trial in healthy volunteers. In the Phase 1 trial to date, PLX5568 has demonstrated attractive PK properties and has been well tolerated. Targeted exposures for human efficacy in pain have been achieved.

In November 2008, Plexxikon signed an agreement with Roche to collaborate in the development of PLX5568, and in the development of other selective Raf inhibitors, for PKD, pain and other indications.



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