Novel Inhibitors Of Endocannabinoid Inactivation for Treatment of Pain, Anxiety and Depression

Tech ID: 24262 / UC Case 2001-104-0

SUMMARY

Bioactive lipids, including anandamide (AEA), are important signaling molecules in humans. Acting through CB_1 cannabinoid receptors in the brain and peripheral tissues, the local concentrations of these lipids have effects on several areas of human health including pain sensation, inflammation, appetite regulation, anxiety, and depression. The regulation of these lipids is partially controlled by their degradation rate by the enzyme fatty acid amide hydrolase (FAAH).

The present portfolio of inventions provides novel small-molecule inhibitors FAAH, including molecules that are limited to peripheral FAAH inhibition as well as molecules improved for oral bioavailability. These compounds have been tested in a number of animal models and one molecule has entered clinical trials in humans. This portfolio includes molecules with IC50 values at single digit nanomolar and in some cases, less than 1.0 nanomolar concentrations *in vitro.*

HIGHLIGHTS OF THE PROJECT

- Less than single digit nanomolar potency *in vitro* against FAAH activity.
- SAR studies have been conducted revealing critical structural features associated with FAAH inhibition, both globally and molecules limited to peripheral FAAH inhibition.
- All compounds are new chemical entities.
- Animal models have been completed in a number of therapeutic areas including pain, anxiety, and depression. Additional animal models have shown FAAH inhibitors to be non-addictive.
- Substantial preclinical de-risking data is available for select compounds.
- Worldwide composition of matter patent claims issued and pending.
- Funding is secured to begin clinical trials in humans for PTSD.
- Useful in treating pain, gastrointestinal NSAID toxicity, anxiety, and depression.

We are currently looking for commercial partners to further develop these FAAH inhibitors for treatment of post-operative pain, and other disorders in which modulation of the levels of OEA, AEA or PEA are clinically relevant.

PUBLICATIONS

- Peripheral gating of pain signals by endogenous lipid mediators. *Nat Neurosci* 2014 Feb;17(2):164-74 PubmedID: 24473264
- Anandamide suppresses pain initiation through a peripheral endocannabinoid mechanism. *Nat Neurosci* 2010 Oct;13(10):1265-70 PubmedID: 20852626
- Pharmacological profile of the selective FAAH inhibitor KDS-4103 (URB597). *CNS Drug Rev* 2006 Spring;12(1):21-38 PubmedID: 16834756

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INVENTORS

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OTHER INFORMATION

KEYWORDS

FAAH, endocannabinoid, PTSD

CATEGORIZED AS

- **Biotechnology**
  - Health
- **Medical**
  - Disease: Autoimmune and Inflammation
  - Disease: Central Nervous System

» Disease: Substance Abuse

» New Chemical Entities, Drug Leads

» Therapeutics

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	7,176,201	02/13/2007	2001-104

RELATED CASES

2001-104-0, 2008-522-0, 2012-075-0, 2013-803-0, 2014-360-0

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Therapy to improve survival in patients with end stage renal disease
- Novel Inhibitors of N-Acylethanolamine-Hydrolyzing Acid Amidase (NAAA)
- Novel Acid Ceramidase Inhibitors for Oncology and Hyperproliferative Skin Disorders

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