ML351 As Treatment For Stroke And Ischemic Brain Injury

Tech ID: 33275 / UC Case 2016-385-0

BACKGROUND

Lipoxygenases form a large family of enzymes capable of oxidizing arachidonic acid and related polyunsaturated fatty acids. One such lipoxygenase, 12/15 LOX can oxidize both the C-12 and C-15 of arachidonic acid, forming 12- or 15-hydroperosyarachidonic acid (12- or 15-HPETE). Lipoxygenases and their metabolites have been implicated in many diseases. In particular 12/15-LOX (also known as 15-LOX-1, 15-LOX, or 15-LO-1 in humans and L-12-LoX, leukocyte-type 12-LO, or L-12-LO in mice) plays a role in atherogenesis, diabetes, Alzheimer's, newborn periventricular leukomalacia, breast cancer, and stroke. Whatever the name, the protein is encoded by the gene ALOX15 in both mice and humans.

Lox inhibitors are difficult to develop due to the mouse and human homologs having different substrate and inhibitor specificities - 12/15 LOX produces predominantly 15-HETE in humans and 12-HETE in mice. So existing inhibitors are not selective for 12/15 LOX with regard to other LOX isoforms. In addition, many are strong antioxidants and therefore may result in off-target effects.

TECHNOLOGY DESCRIPTION

A collaboration between UC Santa Cruz, Boston Children's Hospital, and the National Institutes of Health performed a systematic chemical screen for 12-LOX inhibitors. The screen revealed a family of compounds that exhibit inhibitory effects on 12/15-lipoxygenase. Accordingly, the present invention relates to the use of these compounds for the inhibition of 12/15-lipoxygenase and for the treatment of a condition involving 12/15-lipoxygenase. Exemplary conditions include, but are not limited to, stroke, periventricular leukomalacia, cardiac arrest with resuscitation, atherosclerosis, Parkinson's disease, Alzheimer's disease, and breast cancer.

Issued patents include methods and compounds

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INVENTORS

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OTHER INFORMATION

KEYWORDS

12/15-LOX, 12/15-Lipoxygenase, Lipoxygenase, Arachidonic Acid, HETE, 12-HETE, 15-HETE, Diabetes, Atherogenesis, Alzheimer's, Cardiac arrest, Atherosclerosis, Parkinson's disease, Breast Cancer, Stroke, Newborn periventricular leukomalacia

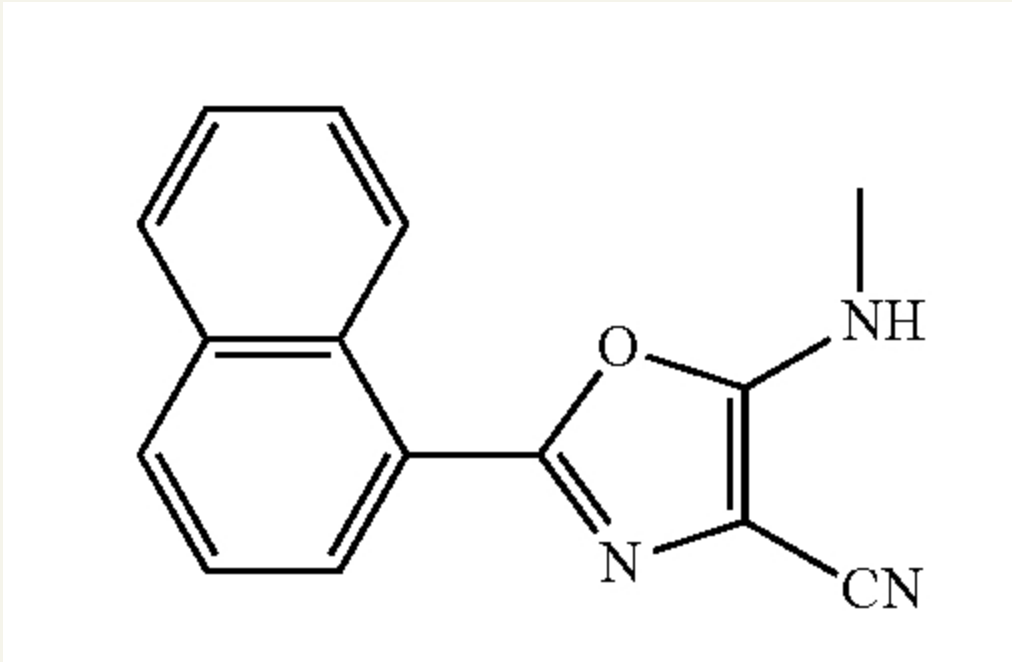
CATEGORIZED AS

- **Medical**
  - Disease: Cancer
  - Disease: Cardiovascular and Circulatory System
  - Disease: Central Nervous System
  - Therapeutics

RELATED CASES

2016-385-0

Structure of lead compound: ML351



APPLICATIONS

Potential therepeutic for:

- diabetes,
- Alzheimer's,
- newborn periventricular leukomalacia,
- breast cancer,
- stroke
- atherogenesis

Inhibition of 12/15 lipoxygenase

ADVANTAGES

- Specifically inhibits 12/15-LOX realtive to 15-LOX, 12-LOX, and 5-LOX
- Low antioxidant activity
- Activity in animal models (e.g. protective in stroke model)
- Good in vivo ADME profile
- Good brain/plasma ratio (crosses BBB)

INTELLECTUAL PROPERTY INFORMATION

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	10,287,279	05/14/2019	2016-385
European Patent Office	Published Application	3036226	06/29/2016	2016-385
Canada	Published Application	2015/027146 A1	02/26/2015	2016-385
Switzerland	Published Application			2016-385
Germany	Published Application			2016-385
France	Published Application			2016-385
United Kingdom	Published Application			2016-385

RELATED MATERIALS

- Discovery of ML351, a Potent and Selective Inhibitor of Human 15-Lipoxygenase-1 - 01/13/2014

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- 15Lox1 Inhibitors For Stroke

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