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## 15Lox1 Inhibitors For Stroke

Tech ID: 33579 / UC Case 2021-597-0

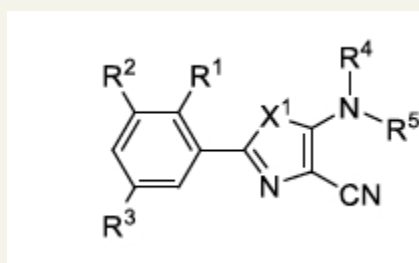
### BACKGROUND

Stroke is a leading cause of mortality and disability worldwide and the economic costs of treatment and post-stroke care are substantial. Every year, more than 14 million people are affected by stroke, and over 6 million stroke patients die from this condition and associated complications.

2-(2,3,5-trisubstituted phenyl)oxazole compounds potently inhibit 12/15-LOX. Hence, the compounds of this disclosure are advantageously useful to treat or prevent various disorders where 12/15-LOX is implicated in the pathology of the disorder (e.g., stroke).

### TECHNOLOGY DESCRIPTION

In collaboration with researchers at Partners Healthcare, UCSC Researchers helped develop compounds that inhibit 12/15 Lipoxygenase



X1 is selected from O and S;

R<sub>1</sub>, R<sub>2</sub>, and R<sub>3</sub> are each independently selected from halo, CN, C<sub>1-3</sub> alkyl, C<sub>1-3</sub> haloalkyl, C<sub>1-3</sub> alkoxy, and C<sub>1-3</sub> haloalkoxy;

R<sub>4</sub> is selected from H, C<sub>1-3</sub> alkyl, and HO-C<sub>1-3</sub> alkylene;

R<sub>5</sub> is selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C(O)OR<sub>a1</sub>, C(O)N(R<sub>a1</sub>)<sub>2</sub>, P(=O)(OR<sub>a1</sub>)<sub>2</sub>, and C(O)R<sub>b1</sub>;

wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl and C<sub>2-6</sub> alkynyl are each optionally substituted with a substituent selected from OR<sub>a1</sub> and OP(=O)(OR<sub>a1</sub>)<sub>2</sub>;

each R<sub>a1</sub> is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>6-10</sub> aryl, C<sub>1-6</sub> alkyl-C<sub>6-10</sub> aryl, and C<sub>1-6</sub> alkyl-C<sub>6-10</sub> aryl-C<sub>1-6</sub> alkyl, wherein said C<sub>1-6</sub> alkyl, C<sub>6-10</sub> aryl,

C<sub>1-6</sub> alkyl-C<sub>6-10</sub> aryl, and C<sub>1-6</sub> alkyl-C<sub>6-10</sub> aryl-C<sub>1-6</sub> alkyl are each optionally substituted with a substituent selected from amino, C<sub>1-6</sub> alkylamino, (C<sub>1-6</sub> haloalkyl)amino, di(C<sub>1-6</sub> alkyl)amino, (C<sub>1-6</sub> alkyl)(C<sub>1-6</sub> haloalkyl)amino, (C<sub>1-6</sub> aryl)amino, (C<sub>6-10</sub> aryl)(C<sub>1-6</sub> alkyl)amino, (5-6-membered heteroaryl)amino, (5-6-membered heteroaryl)(C<sub>1-6</sub>

### CONTACT

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### INVENTORS

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### OTHER INFORMATION

#### KEYWORDS

12/15-LOX, Lipoxygenase,  
Lipoxygenase inhibitors, Stroke,  
Ischemia-Reperfusion Injury,  
Subarachnoid hemorrhage, 12/15-  
Lipoxygenase

#### CATEGORIZED AS

- ▶ **Medical**
  - ▶ Disease: Cardiovascular and Circulatory System
  - ▶ Therapeutics

#### RELATED CASES

2021-597-0, 2020-252-0, 2016-385-  
0, 2021-934-0, 2022-800-0

alkyl)amino, C<sub>6-10</sub> aryl, 4-6 membered heterocycloalkyl, 5-6-membered heteroaryl, and OR<sub>a2</sub>, wherein said C<sub>6-10</sub> aryl, 4-6 membered heterocycloalkyl, and 5-6-membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from amino, C<sub>1-6</sub> alkylamino, di(C<sub>1-6</sub> alkyl)amino, carboxy, and halo; each R<sub>a2</sub> is independently selected from H, C<sub>1-3</sub> alkyl, C<sub>1-3</sub> haloalkyl, C<sub>1-3</sub> alkoxy-C<sub>1-3</sub> alkyl, 4-7 membered heterocycloalkyl-C<sub>1-3</sub> alkyl, 5-6-membered heteroaryloxy-C<sub>1-3</sub> alkyl, C<sub>6-10</sub> aryl, and 5-6-membered heteroaryl, wherein said C<sub>6-10</sub> aryl and 5-6-membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-3</sub> alkoxy, C<sub>1-3</sub> haloalkoxy, C<sub>1-3</sub> alkyl, and C<sub>1-3</sub> haloalkyl; and R<sub>b1</sub> is C<sub>1-6</sub> alkyl, optionally substituted with a substituent selected from amino, C<sub>1-6</sub> alkylamino, di(C<sub>1-6</sub> alkyl)amino, and 4-7 membered heterocycloalkyl ring comprising at least one N atom.

In some embodiments, X<sub>1</sub> is O.

In some embodiments, X<sub>1</sub> is S.

Compounds demonstrated excellent solubility and specificity for 12/15 LOX, metabolic stability in human, mouse, and rat liver endosomes, and significant infarct size reduction in an MCAO ischemia/reperfusion injury mouse model as well as improved behavioral outcomes in a subarachnoid hemorrhage mouse model.

## APPLICATIONS

Treatment of stroke, ischemia reperfusion injury, and subarachnoid hemorrhage.

## ADVANTAGES

Improved solubility and specificity over other 12/15 LOX inhibitors.

Results demonstrated in animal studies.

## INTELLECTUAL PROPERTY INFORMATION

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	<a href="#">10,287,279</a>	05/14/2019	2016-385
European Patent Office	Published Application	4558508	05/28/2025	2022-800
United States Of America	Published Application	<a href="#">2024-033664</a>	10/10/2024	2021-597
Japan	Published Application	2024-531142	08/29/2024	2021-597
European Patent Office	Published Application	4384161	06/19/2024	2021-597
European Patent Office	Published Application	4377297	06/05/2024	2021-934
India	Published Application	202417016587A	03/15/2024	2021-597
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
European Patent Office	Published Application			2020-252
Canada	Published Application			2021-597
China	Published Application			2021-597
Israel	Published Application			2021-597
Republic Of Korea (South Korea)	Published Application			2021-597
Patent Cooperation Treaty	Reference for National Filings	<a href="#">WO 2022/236086</a>	11/10/2022	2020-252

## RELATED MATERIALS

- ▶ [Contributions of 12/15-Lipoxygenase to Bleeding in the Brain Following Ischemic Stroke - 09/28/2019](#)

## RELATED TECHNOLOGIES

- ▶ [ML351 As Treatment For Stroke And Ischemic Brain Injury](#)

## ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- ▶ [ML351 As Treatment For Stroke And Ischemic Brain Injury](#)

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