Potent TMEM16A Small Molecule Treatment for Inflammatory and Reactive Airway Diseases, Asthma, Hypertension, Pain and Cancer

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CONTACT

Todd M. Pazdera
todd.pazdera@ucsf.edu
tel: 415-502-1636.

INVENTORS

- Anderson, Marc O.
- Phuan, Puay-Wah
- Verkman, Alan S.

OTHER INFORMATION

KEYWORDS

Thiophene-arylamides,

AACT, TMEM16A inhibitors,

Ca2+-activated Cl- channel inhibitors

CATEGORIZED AS

- **Medical**
  - Disease: Cancer
  - Disease: Cardiovascular and Circulatory System
  - Disease: Digestive System
  - Disease: Respiratory and Pulmonary System
  - Therapeutics

INVENTION NOVELTY

A novel class of 2-acylamino-cycloalkylthiophene-3-carboxylic acid arylamides (AACTs) as potent TMEM16A inhibitors

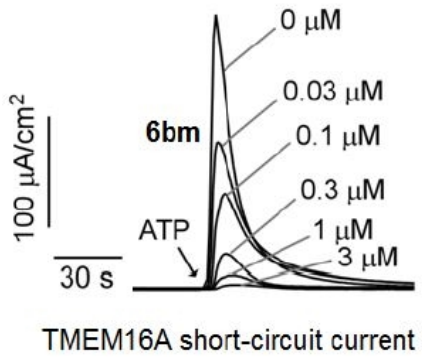
RELATED CASES

2017-138-0

VALUE PROPOSITION

Transmembrane protein 16A (TMEM16A), also called anoctamin 1 (ANO1), is a Ca^{2+}-activated Cl^- channel expressed widely in mammalian epithelia, vascular smooth muscle and electrically excitable cells. Increased TMEM16A expression is associated with COPD and asthma, and TMEM16A is reported as a biomarker for gastrointestinal stromal and esophageal tumors. Pharmacological TMEM16A inhibitors, including the AACT small molecule scaffolds described in this invention, could be used to treat diseases such as inflammatory and reactive airway diseases, hypertension, gastrointestinal hypermotility and some cancers.
The TMEM16A inhibitors developed by UCSF scientists have the following advantages:

- IC_{50} ~ 30 nM; substantially more potent than prior compounds
- Substantially better metabolic stability and PK than prior compounds
- Demonstrated efficacy in acute hypertension, inhibition of intestinal smooth muscle contraction and inhibition of GI tumor cell growth



TMEM16A short-circuit current

TECHNOLOGY DESCRIPTION

The Verkman lab at the University of California, San Francisco has discovered, synthesized and biochemically evaluated of a series of TMEM16A inhibitors. The chemical structure of the 2-acylamino-cycloalkylthiophene-3-carboxylic acid arylamide inhibitor scaffold was refined through medicinal chemistry to identify bromodifluoroacetamide-based inhibitors with enhanced potency and metabolic stability.

LOOKING FOR PARTNERS

To develop & commercialize the TMEM16A inhibitors as therapies for inflammatory and reactive airway diseases, hypertension, gastrointestinal hypermotility and some cancers.

STAGE OF DEVELOPMENT

Proof of Concept – in vitro and ex vivo

DATA AVAILABILITY

Under NCD/CDA

RELATED MATERIALS

- "Substituted 2-Acylaminocycloalkylthiophene-3-carboxylic Acid Arylamides as Inhibitors of the Calcium-Activated Chloride Channel Transmembrane Protein 16A (TMEM16A)." Truong, Eric C., et al., Journal of medicinal chemistry 60.11 (2017): 4626-4635.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	11,358,947	06/14/2022	2017-138

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- SALT-SPARING UREA TRANSPORT INHIBITOR DIURETICS FOR TREATMENT OF CARDIOVASCULAR AND RENAL DISORDERS
- Novel Small Molecule Drug for the Treatment of Constipation and Oxalate Kidney Stones
- Small Molecule Pendrin Inhibitors for Treatment of Inflammatory Airway Diseases and Diuretic Resistance
- Immunotherapy for Treatment of Neuromyelitis Optica (NMO)

ADDRESS

UCSF

Innovation Ventures

600 16th St, Genentech Hall, S-272,

San Francisco,CA 94158

CONTACT

Tel:

innovation@ucsf.edu

https://innovation.ucsf.edu

Fax: