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Novel Acid Ceramidase Inhibitors for Oncology and Hyperproliferative Skin Disorders

Tech ID: 24060 / UC Case 2011-765-0

SUMMARY

Acid ceramidase (AC) catalyzes the hydrolysis of the lipid messenger ceramide thereby regulating ceramide levels in cells. AC is involved in multiple physiological and pathological processes, including cancer resistance and neuropathic pain. Previous AC inhibitors are ceramide analogs with weak inhibitory activity *in vitro* and virtually no utility *in vivo*.

The present portfolio of inventions provides two chemically distinct classes of small-molecule inhibitors of intracellular AC activity, which act at single digit nanomolar concentrations *in vitro* and at low doses *in*

HIGHLIGHTS OF THE PROJECT

- » Single digit nanomolar potency *in vitro* against AC activity.
- » SAR studies reveal critical structural features associated with AC inhibition.
- » All compounds are new chemical entities.
- » Promising hits have been advanced to *in vivo* models of cancers (melanoma, colon) and proliferative diseases of the skin.
- » Worldwide composition of matter patent claims pending.
- » Useful in treating diseases or disorders involving cell over proliferation and/or dysfunctional sphingolipid signal transduction.
- » Compounds useful to sensitize tumor cells to current anticancer drugs and radiation therapy (can increase potency of standard chemotherapies 10-20X).

We are currently looking for commercial partners to further develop these AC inhibitors for treatment of cancers and other disorders in which modulation of the levels of ceramide is clinically relevant.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	0001411588	10/30/2014	2011-765

PUBLICATIONS

Discovery of a New Class of Highly Potent Inhibitors of Acid Ceramidase: Synthesis and Structure-Activity

CONTACT

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INVENTORS

- » Piomelli, Daniele

OTHER INFORMATION

KEYWORDS

Oncology, Cancer, Pain, Acid Ceramidase

CATEGORIZED AS

- » **Biotechnology**
- » Health
- » **Medical**
- » Disease: Cancer
- » Disease: Central Nervous System
- » New Chemical Entities, Drug Leads
- » Therapeutics

Relationship (SAR). *J. Med. Chem.*, 2013, 56(9):3518-3530 **PubmedID: 23614460**

Discovery of highly potent acid ceramidase inhibitors with in vitro tumor chemosensitizing activity. *Sci Rep.* 2013; 3: 1035. **PubmedID: 23301156**

Benzoxazolone Carboxamides: Potent and Systemically Active Inhibitors of Intracellular Acid Ceramidase. *Angew Chem* 2014 Nov 13. doi: 10.1002/anie.201409042.

RELATED CASES

2011-765-0, 2011-765-0

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- ▶ Novel Inhibitors Of Endocannabinoid Inactivation for Treatment of Pain, Anxiety and Depression
- ▶ Therapy to improve survival in patients with end stage renal disease
- ▶ Novel Inhibitors of N-Acylethanolamine-Hydrolyzing Acid Amidase (NAAA)

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