SCIENTIFIC RESEARCH & INTELLECTUAL PROPERTY: TALES FROM THE BENCH

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DEPARTMENT OF CHEMISTRY
UNIVERSITY OF BUEA
June 28, 2019

IL EST QUAND MEME QUI?

1. US Patent Appl. No. 13/420,479 of March 14/2012 - ***Methods and Compositions for Preparing Noribogaine from Voacangine.*** Robert M. Moriarty & Simon Mbua Ngale Efange.

2. US patent No. 6,846,817B2 (25/01/2005) – ***Nicotine Receptor Ligands;*** Inventor: Simon Mbua Ngale Efange.

3. US Patent No. 5,948,807 (07/09/1999) – ***Spiroindanamines and Spiroindanamides;*** Inventors: Simon Mbua Ngale Efange & Deborah C. Mash.

4. US Patent No. 5,929,087 (27/07/1999) - ***Decahydroquinoline-based anti-cholinergic agents;*** Inventors: Simon Efange and Stanley Parsons.

5. US Patent No. 5,876,694 (02/03/1999)– ***Azavesamicols;*** **Inventors:** Simon Mbua Ngale Efange & Stanley M. Parsons.

LIST OF PATENTS-2

6. US Patent No. 5,789,420 (04/08/1998) – ***Azavesamicols.*** Simon Mbua Ngale Efange & Stanley M. Parsons

7. US Patent No. 5,721,243 (24/02/1998) – ***Radiopharmaceutical Agents for the Detection of Alzheimer's Disease.*** Simon Mbua Ngale Efange & Stanley M. Parsons

8. US Patent No. 5,616,575 (01/04/1997) – ***Bioactive Tricyclic Analogs.*** Simon Mbua Ngale Efange and Deborah C. Mash.

9. US Patent No. 5,554,752 (10/09/1996) – ***Spirovesamicols.*** Simon Efange and Stanley Parsons

10. US Patent No. 5,457,207 (10/10/1995) – ***Spirovesamicols.*** Simon Mbua Ngale Efange & Stanley M. Parsons.

LIST OF PATENTS-3

11. US Patent No. 5,358,712 (10/25/94) – ***Radiopharmaceutical Agents for the Detection of Alzheimer's Disease; Inventors:*** Simon Mbua Ngale Efange & Stanley M. Parsons.

12. US Patent No. 5,338,852 (16/08/1994) – ***Azavesamicols;*** Inventors: Simon Mbua Ngale Efange & Stanley M. Parsons.

13. US Patent No. 4,895,937 (01/23/90) – ***5-Iodo-2-pyrimidinone nucleoside;*** Inventors: Thomas J. Bardos, Yung-Chi Cheng, Alan C. Schroeder & Simon Mbua Ngale Efange.

14. US Patent No. 4,782,142 (11/01/88) - ***Novel 5-substituted 2-pyrimidinone nucleosides and methods of use; Inventors:*** Thomas J. Bardos, Yung-Chi Cheng, Alan C. Schroeder & Simon Mbua Ngale Efange.

WHO ARE WE?

The University

- Teaching
- Research
- Outreach

WHAT IS OUR BUSINESS?

KNOWLEDGE

- Dissemination of knowledge
- Generation of new knowledge (Research)

WHAT IS RESEARCH?

"…any gathering of data, information and facts for the advancement of knowledge."

"…performing a *methodical study* in order to *prove a hypothesis or answer a specific question.*"

WHAT ARE THE OUTCOMES OF RESEARCH?

- New molecules, designs, devices
- New methods
- New software
- New data

WHERE ARE WE IN THE LARGER PICTURE?

GLOBAL INNOVATION INDEX -2018 (WIPO)

1. Switzerland
2. Netherlands
3. Sweden
4. United Kingdom
5. Singapore
6. U.S.A

57. India
58. South Africa
111. Cameroon
118. Nigeria

WHERE ARE WE IN THE LARGER PICTURE?

(THE MEANS)

UNIVERSITY OF MINNESOTA 2018 OPERATING BUDGET

$3.8 billion (approx. 2,181.2 billion FCFA);

Research $302.9 million (173.86 billion FCFA)

REPUBLIC OF CAMEROON - 2019 STATE BUDGET

Amt: 4,850.5 billion FCFA

MINESUP 2019 BUDGET – 55.95 billion FCFA

MINRESI 2019 BUDGET – 11.92 billion FCFA

WHAT MUST WE DO TO MAKE A DIFFERENCE?

- CREATE AND INNOVATE
- RE-THINK OUR APPROACH TO RESEARCH

(tunnel vision; 1-dimensional)

"Trop de chercheurs, pas de trouveurs."

MESSAGE

Your ideas may be worth more than the paper they are written on, but you must be prepared to *work harder.*

HOW MAY WE BENEFIT FROM OUR IDEAS & INNOVATIONS?

INTELLECTUAL PROPERTY (IP)

A category of property that includes intangible creations of the human intellect.

HOW IS IP PROTECTED?

IP RIGHTS

Rights that are had by a person or by a company to have exclusive **rights** to use its own plans, ideas, or other intangible assets without the worry of competition, at least for a specific period of time.

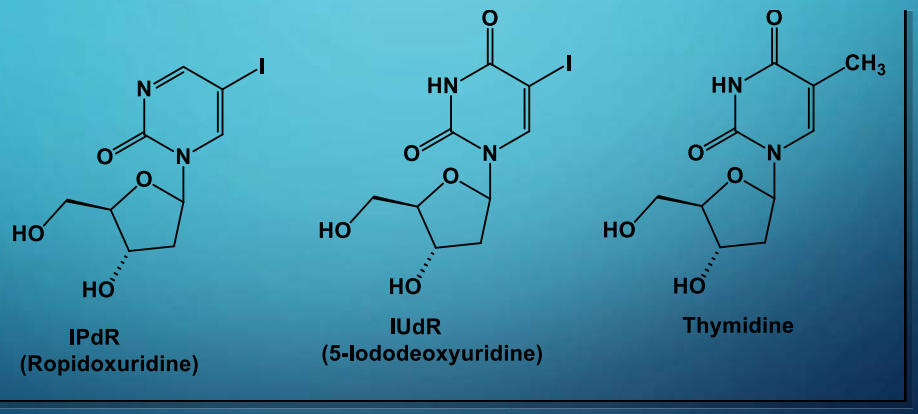
HOW IS IP CLASSIFIED?

- Trade Secrets
- Trademarks.
- Copyrights
- Patents

HOW DO WE PROCEED TO ACQUIRE IP?
CREATE! INNOVATE!

- CONCEPTUALIZATION
- DISCLOSURE *(Publish or Protect?)*
- PATENT APPLICATION (Costs and other considerations)
- COMMERCIALIZATION (Search for sponsors, licensees, ownership, benefits sharing etc.)
- PATENT MAINTENANCE

THE CASE OF ROPIDOXURIDINE



The Case of IPdR *(Ropidoxuridine)*

- Synthesized 1982/83 (Efange et al., J. Med. Chem. 28:904-910, 1985)
- Anti-herpes activity confirmed in 1983
- Scale-up work in 1984
- GD Searle
- Monsanto
- Hana Biosciences
- Shuttle Pharmaceuticals Inc.

ROPIDOXURIDINE

US4895937.pdf

United States Patent [19]
Bardos et al.

[11] **Patent Number: 4,895,937**
[45] **Date of Patent: Jan. 23, 1990**

[54] **5-IOSO-2-PYRIMIDINONE NUCLEOSIDE**

[75] Inventors: **Thomas J. Bardos**, Snyder, N.Y.; **Yung-Chi Cheng**, Chapel Hill, N.C.; **Alan C. Schroeder**, Silver Springs, Md.; **Simon M. N. Efange**, Plymouth, Minn.

[73] Assignee: **The Research Foundation of State University of New York**, Albany, N.Y.

[21] Appl. No.: **263,183**

[22] Filed: **Oct. 27, 1988**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 641,770, Aug. 20, 1984, Pat. No. 4,782,142, which is a continuation-in-part of Ser. No. 337,297, Jan. 5, 1982, Pat. No. 4,468,384.

[51] **Int. Cl.**[4] **C07H 19/067**
[52] **U.S. Cl.** **536/23**
[58] **Field of Search** 536/23; 514/49

[56] **References Cited**

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134429 2/1979 German Democratic Rep. .

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Oftebro, R. et al, Biochemical Pharmacology, vol. 21, pp. 2451–2456, Pergamon Press, 1972.
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McCormack, J. J., et al., Biochemical Pharmacology, vol., 29, pp. 830–832, 1980.
Goodman & Gilman, The Pharmacological Basis of Therapeutics, (1980) pp. 1240–1241.
Prusoff, W. H., et al., Antiviral Research, 4, pp. 303–315, Elsevier, 1984.

Primary Examiner—Blondel Hazel
Attorney, Agent, or Firm—Howard M. Ellis; Michael L. Dunn

[57] **ABSTRACT**

The nuceoside 1-(2-Deoxy-β-D-ribofuranosyl)-5-(iodo)-2-pyrimidinone possesses a high level of antiviral activity and a low level of toxicity to the host cell making it an especially effective therapeutic agent for HSV-2.

1 Claim, No Drawings

ROPIDOXURIDINE

Shuttle Pharmaceuticals...
https://www.shuttlepharma.com

Shuttle Pharmaceuticals Holdings, Inc.

Home | Company | Technology | Investors

To improve the safety, efficacy and quality of life of cancer patients undergoing radiation therapy.

About Us

Shuttle Pharmaceuticals Holdings, Inc., through our subsidiary, Shuttle Pharmaceuticals, Inc., is developing first-in-class therapies to improve the outcomes of patients receiving radiation therapy for the treatment of cancers. The focus is on products with unique properties to sensitize cancer cells, protect normal tissues and monitor clinical responses to treatment.

Our Focus

We have built a platform technology to advance the discovery and development of novel small molecules to modify the effects of ionizing radiations on cancer cells and normal tissues. To accomplish this goal, we have developed strategic collaborations to leverage programs that include drug discovery, preclinical studies of radiation sensitizers, protectors and epigenetic therapeutics. A phase I clinical trial of a radiation sensitizer has been initiated.

Market Opportunity

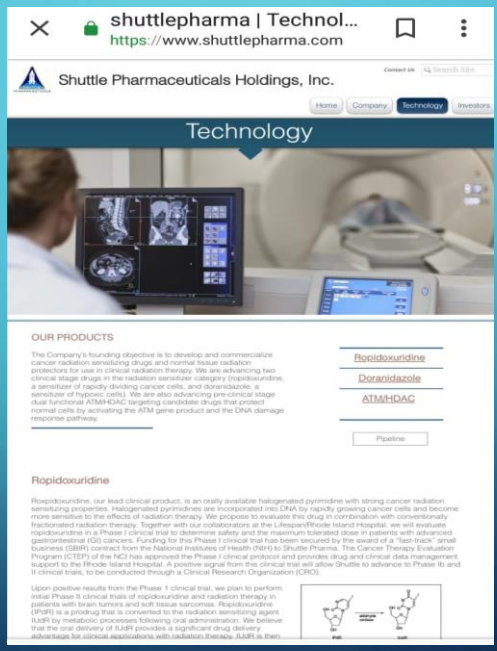
The precision of radiation therapy (RT) delivery has reached a technical plateau, limited only by the tolerance of normal tissues surrounding tumors. Further improvements will come with drugs that modify cellular responses of cancers and normal tissues to radiation.

Unmet Need

A non-cytotoxic radiation sensitizer for use in cancer treatment:

- 60 percent of cancer patients undergo radiation therapy (RT)
- >1 million patients are treated annually in the U.S.
- Annual estimated radiation oncology market is >$4 billion dollars
- Cancer treated with RT include prostate, lung, breast, brain,

ROPIDOXURIDINE



ROPIDOXURIDINE – STILL GOING AFTER ALL THESE YEARS

European Cancer Organization (Dublin, Ireland, November 14, 2018)

"A new drug designed to make radiotherapy more effective in treating cancer has been given to patients while they are receiving radiation and shown to be safe, according to research presented today."

(Wednesday) at the 30th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Dublin, Ireland.

FROM IBOGAINE TO "IBOGANOIDS"

US005616575A

United States Patent [19]
Efange et al.

[11] **Patent Number: 5,616,575**
[45] **Date of Patent: Apr. 1, 1997**

[54] **BIOACTIVE TRICYCLIC IBOGAINE ANALOGS**

[75] Inventors: **S. Mbua N. Efange**, Plymouth, Minn.; **Deborah C. Mash**, North Bay Village, Fla.

[73] Assignees: **Regents of the University of Minnesota**, Minneapolis, Minn.; **University of Miami**, Miami, Fla.

[21] Appl. No.: **567,374**

[22] Filed: **Dec. 4, 1995**

[51] **Int. Cl.**[6] **A61K 31/395**
[52] **U.S. Cl.** **514/215**; 540/586; 514/812
[58] **Field of Search** 514/215, 812; 540/586

[56] **References Cited**

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5,035,878	7/1991	Borch et al.	424/10
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W.L. Woolverton et al., "Neurobiology of Cocaine Abuse," *Trends Pharmacol. Sci.*, 13, 193–200 (1992).
G. Zetler et al., "Cerebral Pharmacokinetics of Tremor–Producing Harmala and Iboga Alkaloids," *Pharmacology*, 7, 237–248 (1972).

Primary Examiner—James H. Reamer
Attorney, Agent, or Firm—Schwegman, Lundberg, Woessner & Kluth, P.A.

[57] **ABSTRACT**

Ibogaine analogs are provided, which are phenyl-substituted-hexahydroazepino[4,5-b]indoles useful to treat cocaine addiction and the use of other addictive substances.

21 Claims, 3 Drawing Sheets

FROM NICOTINE TO CHROMAPROLINE

US006846817B2

(12) **United States Patent**
Efange

(10) **Patent No.: US 6,846,817 B2**
(45) **Date of Patent: Jan. 25, 2005**

(54) **NICOTINE RECEPTOR LIGANDS**

(75) Inventor: **S. Mbua Ngale Efange**, Plymouth, MN (US)

(73) Assignee: **Regents of the University of Minnesota**, Minneapolis, MN (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **08/997,718**

(22) Filed: **Nov. 30, 2001**

(65) **Prior Publication Data**

US 2003/0027860 A1 Feb. 6, 2003

Related U.S. Application Data

(63) Continuation of application No. PCT/US00/13348, filed on Jun. 2, 2000.
(60) Provisional application No. 60/137,099, filed on Jun. 2, 1999.

(51) **Int. Cl.**[7] **C07D 405/04**; A61K 31/453; A61P 25/34

(52) **U.S. Cl.** **514/228.2**; 514/210.19; 514/233.5; 514/256; 514/307; 514/326; 514/337; 514/422; 544/62; 544/131; 544/153; 544/333; 546/525; 546/950; 546/139; 546/144; 546/148; 546/196; 546/282.7; 546/284.1

(58) **Field of Search** 514/210.19, 228.2, 514/233.5, 307, 320, 337, 442, 544/62, 131, 153, 333; 546/144, 139, 148, 196, 282.7, 284.1; 546/525, 950

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(List continued on next page.)

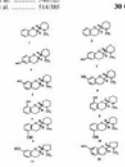
Primary Examiner—Mark L. Berch
(74) *Attorney, Agent, or Firm*—Schwegman, Lundberg, Woessner & Kluth, P.A.

(57) **ABSTRACT**

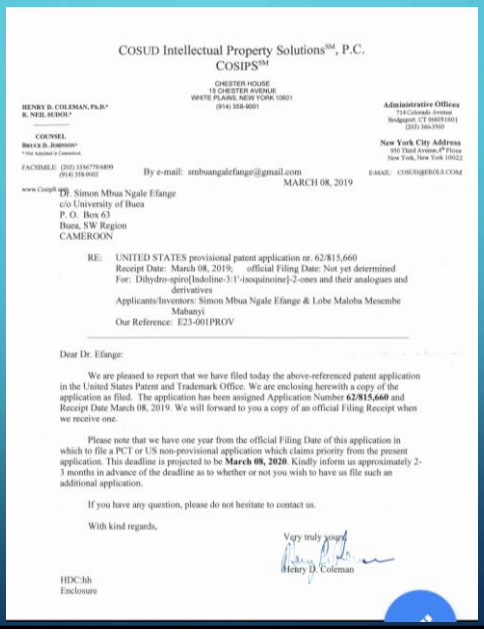
The invention provides nicotine receptor agonists of formula I:

wherein R$_n$, x, y, and n have any of the values given in the specification, or a pharmaceutically acceptable salt thereof, as well as pharmaceutical compositions comprising such a compound or salt, methods for preparing such a compound or salt, and methods for modulating (e.g. antagonizing or activating) nicotine receptors with such a compound or salt.

30 Claims, 13 Drawing Sheets



CAN WE DO IT AT UB?



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MARCH 08, 2019

Dr. Simon Mbua Ngale Efange
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RE: UNITED STATES provisional patent application nr. 62/815,660
Receipt Date: March 08, 2019; official Filing Date: Not yet determined
For: Dihydro-spiro[Indoline-3:1'-isoquinoine]-2-ones and their analogues and derivatives
Applicants/Inventors: Simon Mbua Ngale Efange & Lobe Maloba Mesembe Mabanyi
Our Reference: E23-001PROV

Dear Dr. Efange:

We are pleased to report that we have filed today the above-referenced patent application in the United States Patent and Trademark Office. We are enclosing herewith a copy of the application as filed. The application has been assigned Application Number **62/815,660** and Receipt Date March 08, 2019. We will forward to you a copy of an official Filing Receipt when we receive one.

Please note that we have one year from the official Filing Date of this application in which to file a PCT or US non-provisional application which claims priority from the present application. This deadline is projected to be **March 08, 2020**. Kindly inform us approximately 2-3 months in advance of the deadline as to whether or not you wish to have us file such an additional application.

If you have any question, please do not hesitate to contact us.

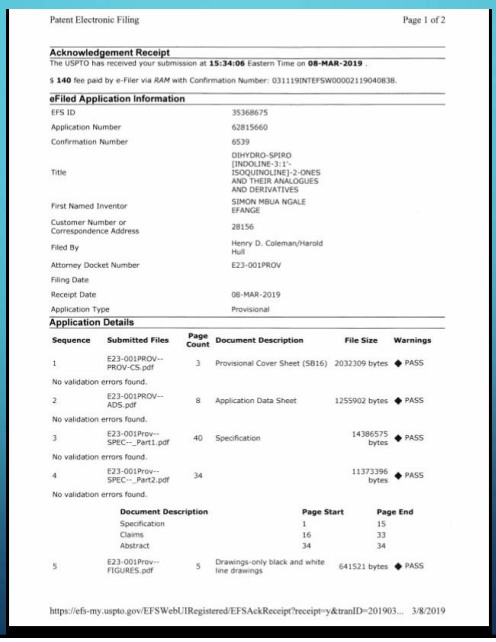
With kind regards,

Very truly yours,

Henry D. Coleman

HDC:hh
Enclosure

CAN WE DO IT AT UB?



Patent Electronic Filing — Page 1 of 2

Acknowledgement Receipt

The USPTO has received your submission at **15:34:06** Eastern Time on **08-MAR-2019** .

$ **140** fee paid by e-Filer via *RAM* with Confirmation Number: 031119INTEFSW00002119040838.

eFiled Application Information

EFS ID	35368675
Application Number	62815660
Confirmation Number	6539
Title	DIHYDRO-SPIRO [INDOLINE-3:1'-ISOQUINOLINE]-2-ONES AND THEIR ANALOGUES AND DERIVATIVES
First Named Inventor	SIMON MBUA NGALE EFANGE
Customer Number or Correspondence Address	28156
Filed By	Henry D. Coleman/Harold Hull
Attorney Docket Number	E23-001PROV
Filing Date	
Receipt Date	08-MAR-2019
Application Type	Provisional

Application Details

Sequence	Submitted Files	Page Count	Document Description	File Size	Warnings
1	E23-001PROV--PROV-CS.pdf	3	Provisional Cover Sheet (SB16)	2032309 bytes	PASS
No validation errors found.					
2	E23-001PROV--ADS.pdf	8	Application Data Sheet	1255902 bytes	PASS
No validation errors found.					
3	E23-001Prov--SPEC--_Part1.pdf	40	Specification	14386575 bytes	PASS
No validation errors found.					
4	E23-001Prov--SPEC--_Part2.pdf	34		11373396 bytes	PASS
No validation errors found.					

Document Description	Page Start	Page End
Specification	1	15
Claims	16	33
Abstract	34	34

5	E23-001Prov--FIGURES.pdf	5	Drawings-only black and white line drawings	641521 bytes	PASS

https://efs-my.uspto.gov/EFSWebUIRegistered/EFSAckReceipt?receipt=y&tranID=201903... 3/8/2019

CAN WE DO IT AT UB?

- Yes, we can, but we must re-shape our attitude to research and innovation.
- We must be prepared to work even harder. Otherwise, we shall be condemned to live with "….*trop de chercheurs, pas de trouveurs*".

PARTING MESSAGE

Your ideas may be worth more than the paper they are written on,

but you must be prepared to work harder.

ACKNOWLEDGEMENTS

- Thomas J. Bardos (deceased), formerly Professor of Medicinal Chemistry & Biochemical Pharmacology, SUNY Buffalo.
- Hank F. Kung (emeritus), Professor of Radiology & Pharmacology, University of Pennsylvania.
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- University of Minnesota Seed Grant Program
- National Parkinson Foundation
- Alzheimer's Disease & Related Diseases Association (ADRDA)
- Nihon Medi-Physics (Japan)
- US SBIR (NovoNeuron)
- UB Research Fund
- MINESUP/Research Modernization Scheme