Introduction to Patents

Rutgers University - Robert Wood Johnson Medical School
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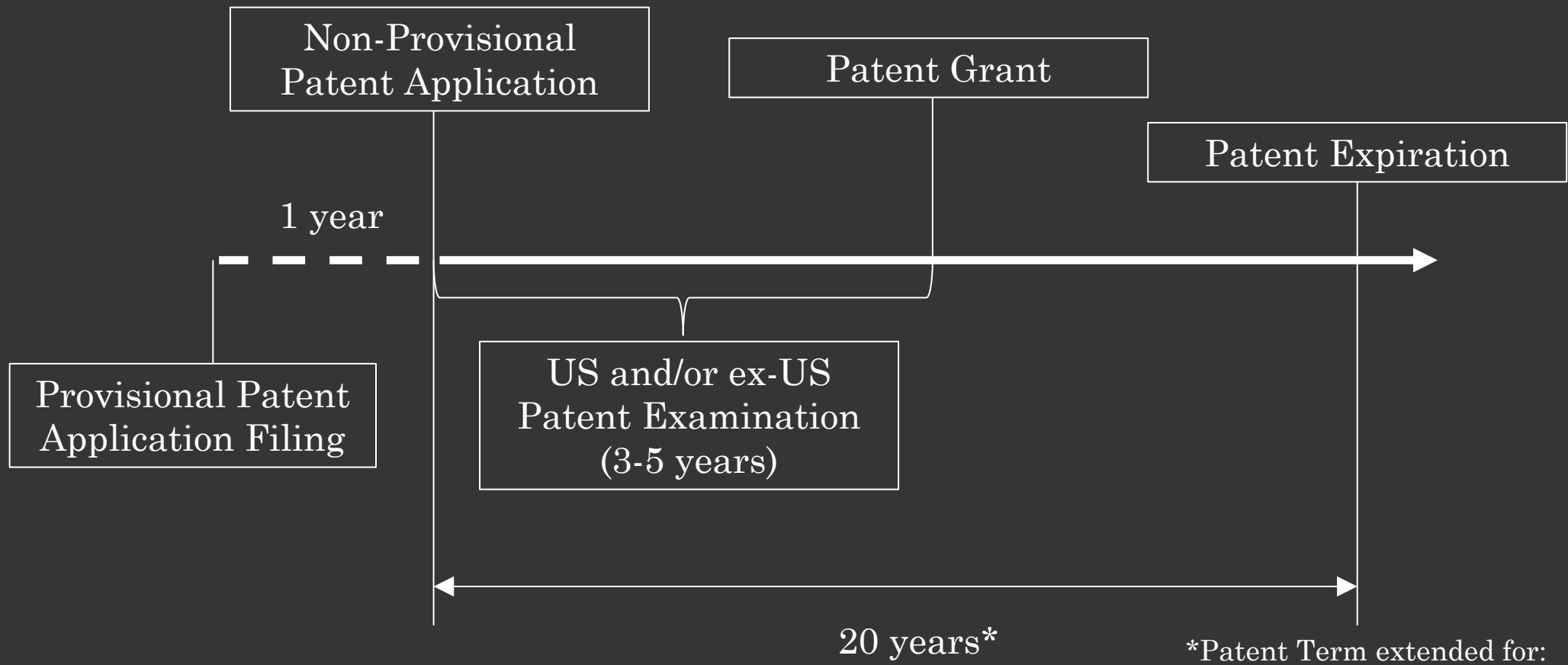
Victor P. Ghidu

Patents and the Patent Process

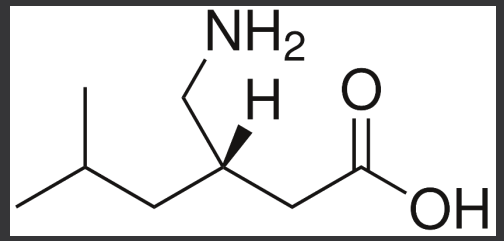
- *A patent provides a right to exclude*
- *What makes an invention patentable? The invention must…*
  - *Encompass "patentable subject matter"*
  - *Be useful*
  - *Be new*
  - *Be non-obvious*
  - *Be supported by a specification containing a written description of the invention, and of the manner and process of making and using it, in such terms as to enable any person skilled in the art to make and use the same, and also set forth the best mode* of carrying out the invention.*

Patents and the Patent Process

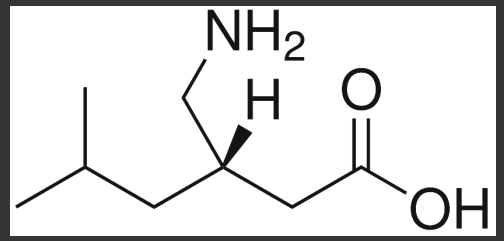


*Patent Term extended for:

1. Patent office delays (PTA)
2. Regulatory Delays (PTE)
3. Pediatric Exclusivity (6 mos.)



- *Pregabalin (LYRICA) – Oral - Pfizer*
  - *Launched in US in 2004;*
  - *Indicated for the treatment of:*
    - *Neuropathic pain associated with diabetic peripheral neuropathy (DPN)*
    - *Postherpetic neuralgia (PHN)*
    - *Adjunctive therapy for the treatment of partial onset seizures in patients 4 years of age and older*
    - *Fibromyalgia*
    - *Neuropathic pain associated with spinal cord injury*



- *Pregabalin (LYRICA) – Oral - Pfizer*
  - *Protected by Orange Book listed patents – all expired.*
  - *Protected by various regulatory exclusivities*
    - *Pediatric Exclusivity*
      - *Added 6 months to patent term*
    - *New Patient Population Exclusivity*
      - *Marketing exclusivity until 2022 for certain indications*

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
003	6001876*PED	06/30/2019					
003	6197819*PED	06/30/2019					
003	RE41920*PED	06/30/2019					

Exclusivity Data

Product No	Exclusivity Code	Exclusivity Expiration
003	M-193INFORMATION ADDED TO THE LABELING REGARDING A 15-WEEK, RANDOMIZED, DOUBLE-BLIND, PARALLEL-GROUP, PLACEBO-CONTROLLED FLEXIBLE-DOSE SAFETY AND EFFICACY STUDY OF PREGABALIN IN ADOLESCENTS (12 THROUGH 17 YEARS OLD) WITH FIBROMYALGIA COMPETITIVE GENERIC THERAPY	12/22/2019
003	M-193INFORMATION ADDED TO THE LABELING REGARDING A 15-WEEK, RANDOMIZED, DOUBLE-BLIND, PARALLEL-GROUP, PLACEBO-CONTROLLED FLEXIBLE-DOSE SAFETY AND EFFICACY STUDY OF PREGABALIN IN ADOLESCENTS (12 THROUGH 17 YEARS OLD) WITH FIBROMYALGIA *PED PEDIATRIC EXCLUSIVITY	06/22/2020
003	NPPNEW PATIENT POPULATION COMPETITIVE GENERIC THERAPY	05/03/2021
003	NPPNEW PATIENT POPULATION *PED PEDIATRIC EXCLUSIVITY	11/03/2021
003	NPPNEW PATIENT POPULATION COMPETITIVE GENERIC THERAPY	05/23/2022
003	NPPNEW PATIENT POPULATION *PED PEDIATRIC EXCLUSIVITY	11/23/2022

United States Patent [19]

Singh

[11] **Patent Number: 6,001,876**

[45] **Date of Patent: Dec. 14, 1999**

[54] **ISOBUTYLGABA AND ITS DERIVATIVES FOR THE TREATMENT OF PAIN**

[75] Inventor: **Lakhbir Singh**, Cambridgeshire, United Kingdom

[73] Assignee: **Warner-Lambert Company**, Morris Plains, N.J.

[21] Appl. No.: **09/043,358**

[22] PCT Filed: **Jul. 16, 1997**

[86] PCT No.: **PCT/US97/12390**

§ 371 Date: **Jul. 15, 1998**

§ 102(e) Date: **Jul. 15, 1998**

[87] PCT Pub. No.: **WO98/03167**

PCT Pub. Date: **Jan. 29, 1998**

Related U.S. Application Data

[60] Provisional application No. 60/022,337, Jul. 24, 1996.

[51] **Int. Cl.**[6] **A61K 31/195**

[52] **U.S. Cl.** **514/561**

[58] **Field of Search** 514/561

[56] **References Cited**

U.S. PATENT DOCUMENTS

5,563,175 10/1996 Silverman et al. 514/561

FOREIGN PATENT DOCUMENTS

9209560 6/1992 WIPO .
9323383 11/1993 WIPO .

Primary Examiner—James H. Reamer
Attorney, Agent, or Firm—Elizabeth M. Anderso

[57] **ABSTRACT**

The instant invention is a method of using certain
glutamic acid and gamma-aminobutyric acid in pai

15 Claims, 18 Drawing Sheets

(12) **United States Patent**
Silverman et al.

(10) **Patent No.: US 6,197,819 B1**

(45) **Date of Patent: Mar. 6, 2001**

(54) **GAMMA AMINO BUTYRIC ACID ANALOGS AND OPTICAL ISOMERS**

(75) Inventors: **Richard B. Silverman**, Morton Grove, IL (US); **Ryszard Andruszkiewicz**, Sopot (PL)

(73) Assignee: **Northwestern University**, Evanston, IL (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.: **08/420,905**

(22) Filed: **Apr. 11, 1995**

Related U.S. Application Data

(63) Continuation of application No. 08/064,285, filed on May 18, 1993, now abandoned, which is a continuation-in-part of application No. 07/886,080, filed on May 20, 1992, now abandoned, which is a continuation-in-part of application No. 07/618,692, filed on Nov. 27, 1990, now abandoned.

(51) **Int. Cl.**[7] **A61K 31/195**

(52) **U.S. Cl.** **514/561**; 562/553

(58) **Field of Search** 562/553; 514/561

Journal of Organic Chemistry, vol. 26, No. 5, May 1961, p. 1685.

Journal of Psychiatric Research, vol. 11, 1974, pp. 255–256.

Tetrahedron Letters, vol. 32, No. 45, Nov. 1991, pp. 6547–6550.

Epilepsy, Harris P. Mawdsley C. eds (1974) Churchill Livingston, Edinburg, pp. 55–64.

Journal of Organic Chemistry, vol. 27 (1962), pp. 2406–2411.

GABA in Nervous System Function, Raven Press, New York (1976), pp. 487–495.

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Fadel et al., (1988) Optically active alpha–alkylsuccinates from the stereoselective alkylation of chiral imide enolates. *Tetrahedron Letters,* vol. 29, No. 48, pp. 6257–6260.

Kim and Cocolas (1965) Glutamic acid analogs. The synthesis of 3–alkylgultamic acids and 4–alkylpyroglutamic acids. *J. Med. Chem.,* vol. 8, No. 4, pp. 509–513.

Mauger (1981) Diastereoisomers of 3–methylpyroglutamic acid and β–methylglutamic acid. *J. Org. Chem.,* 46:1032–1035.

Petter et al., (1990) Inhibition of γ–butyrobetaine hydroxylase by cyclopropyl–substituted γ–butyrobetaines. *J. Org. Chem.,* 55:3088–3097.

Silverman et al., (1991) 3–alkyl–4–aminobuttyric acids: the

United States Patent [19]

Singh

[11] **Patent Number: 6,001,876**

[45] **Date of Patent: Dec. 14, 1999**

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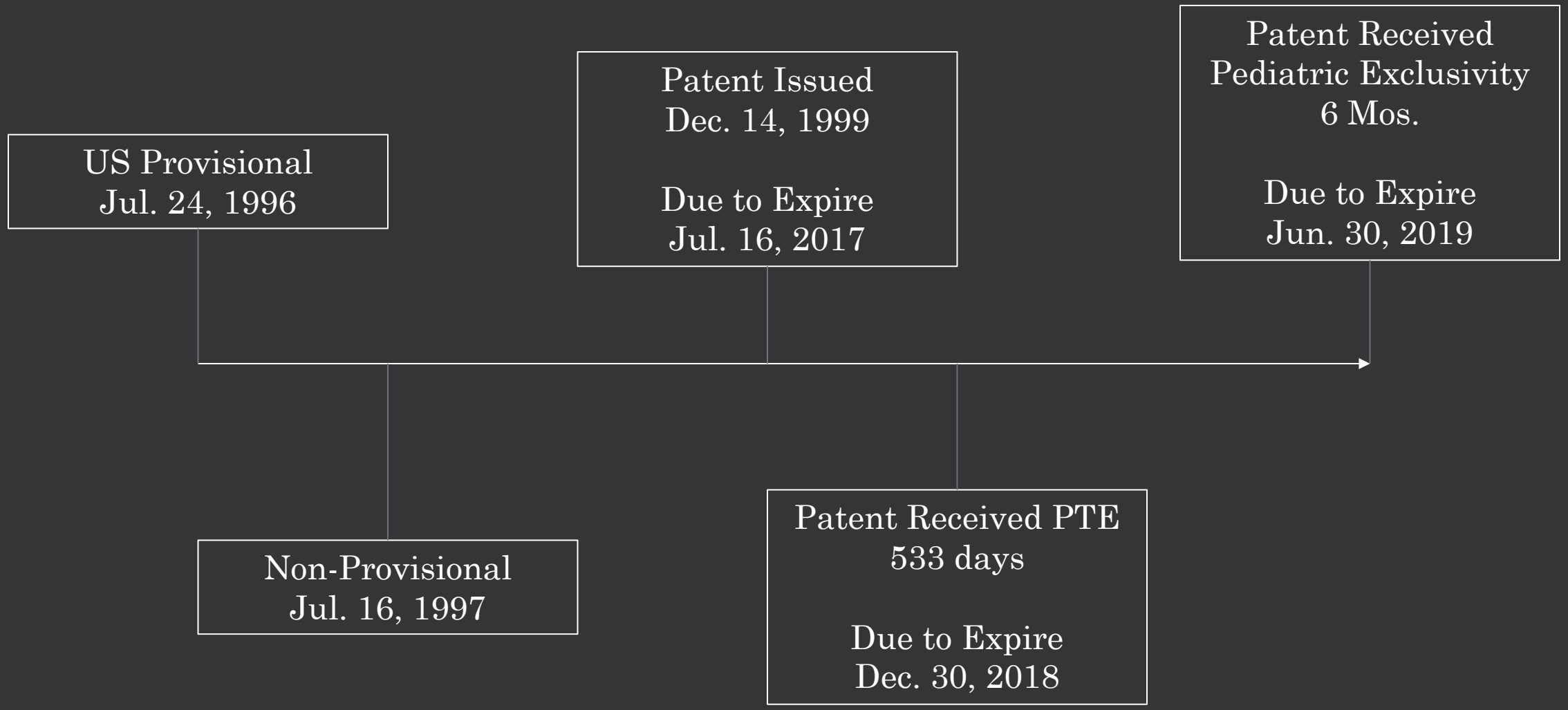
Primary Examiner—James H. Reamer
Attorney, Agent, or Firm—Elizabeth M. Anderson

[57] **ABSTRACT**

The instant invention is a method of using certain analogs of glutamic acid and gamma-aminobutyric acid in pain therapy.

15 Claims, 18 Drawing Sheets

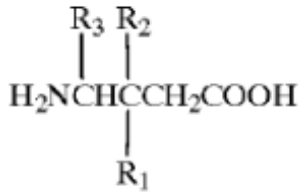
The '876 Patent's Life



What is claimed is:

1. A method for treating pain comprising administering a therapeutically effective amount of a compound of Formula I

I



or a pharmaceutically acceptable salt, diastereomer, or enantiomer thereof wherein

R_1 is a straight or branched alkyl of from 1 to 6 carbon atoms, phenyl, or cycloalkyl of from 3 to 6 carbon atoms;

R_2 is hydrogen or methyl; and

R_3 is hydrogen, methyl, or carboxyl to a mammal in need of said treatment.

2. A method according to claim **1** wherein the compound administered is a compound of Formula I wherein R_3 and R_2 are hydrogen, and R_1 is $—(CH_2)_{0-2}—i\ C_4H_9$ as an (R), (S), or (R,S) isomer.

3. A method according to claim **1** wherein the compound administered is named (S)-3-(aminomethyl)-5-methylhexanoic acid and 3-aminomethyl-5-methyl-hexanoic acid.

4. A method according to claim **1** wherein the pain treated is inflammatory pain.

5. A method according to claim **1** wherein the pain treated is neuropathic pain.

6. A method according to claim **1** wherein the pain treated is cancer pain.

7. A method according to claim **1** wherein the pain treated is postoperative pain.

8. A method according to claim **1** wherein the pain treated is phantom limit pain.

9. A method according to claim **1** wherein the pain treated is bum pain.

10. A method according to claim **1** wherein the pain treated is gout pain.

11. A method according to claim **1** wherein the pain treated is osteoarthritic pain.

12. A method according to claim **1** wherein the pain treated is trigeminal neuralgia pain.

13. A method according to claim **1** wherein the pain treated is acute herpetic and postherpetic pain.

14. A method according to claim **1** wherein the pain treated is causalgia pain.

15. A method according to claim **1** wherein the pain treated is idiopathic pain.

(12) **United States Patent**
Silverman et al.

(10) **Patent No.: US 6,197,819 B1**
(45) **Date of Patent: Mar. 6, 2001**

(54) **GAMMA AMINO BUTYRIC ACID ANALOGS AND OPTICAL ISOMERS**

(75) Inventors: **Richard B. Silverman**, Morton Grove, IL (US); **Ryszard Andruszkiewicz**, Sopot (PL)

(73) Assignee: **Northwestern University**, Evanston, IL (US)

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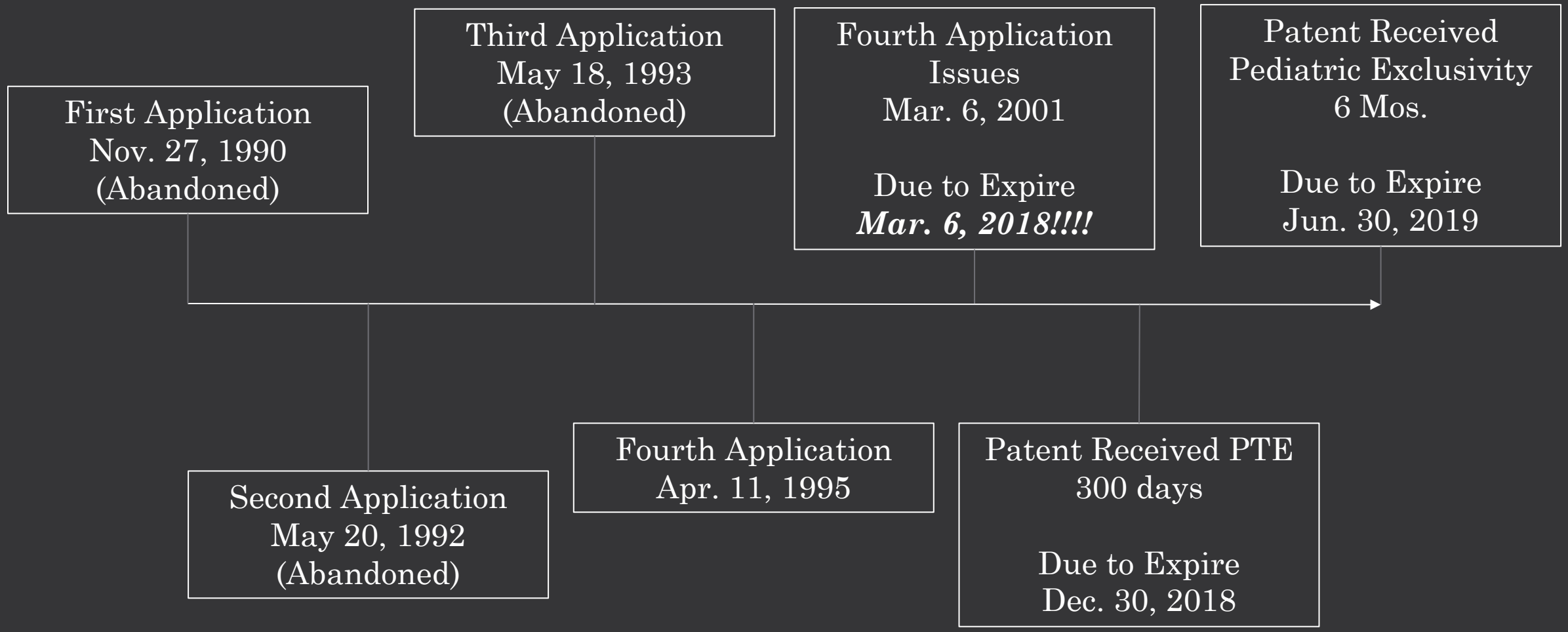
The '819 Patent's Life



What is claimed is:

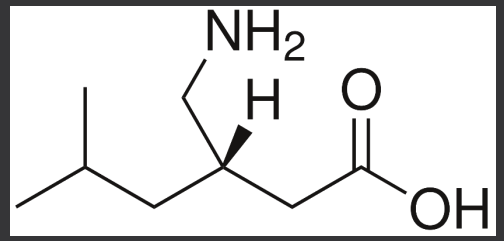
1. A compound of the formula S-(+)-4-amino-3-(2-methylpropyl) butanoic acid as a single optical isomer.

2. 4-amino-3-(2-methylpropyl) butanoic acid, or a pharmaceutically acceptable salt thereof.

3. A pharmaceutically acceptable salt of S-(+)-(4)-amino-3-(2-methylpropyl) butanoic acid, said salt being present as a single optical isomer.

4. A pharmaceutical composition comprising a compound any one of claims **1** or **3**, together with a pharmaceutically acceptable carrier.

* * * * *



- *Pregabalin (LYRICA) – Oral - Pfizer*
  - *Launched in US in 2004*
  - *First Generic Paragraph IV Certifications filed in 2008*
  - *Patents Expired Jun. 30, 2019*
  - *First Group of Generics Approved in Jul. 19, 2019*

1. *What are the differences, if any, in the claims between the two patents.*

2. *If you think there are differences, how does the scope of exclusivity differ between the claims in the '876 patent vs. the claims in the '819 patent?*

3. *Which patent do you think is "stronger"?*

4. *With regard to pharmaceuticals, are patents good, bad, a necessity, a cost of doing business, or something in between?*

Thank You!

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