



US007919499B2

(12) **United States Patent**
Ehrich

(10) **Patent No.:** **US 7,919,499 B2**
(45) **Date of Patent:** **Apr. 5, 2011**

(54) **NALTREXONE LONG ACTING FORMULATIONS AND METHODS OF USE**

(75) Inventor: **Elliot Ehrich**, Lincoln, MA (US)

(73) Assignee: **Alkermes, Inc.**, Waltham, MA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 1673 days.

(21) Appl. No.: **11/083,167**

(22) Filed: **Mar. 17, 2005**

(65) **Prior Publication Data**
US 2005/0245558 A1 Nov. 3, 2005

Related U.S. Application Data

(60) Provisional application No. 60/564,542, filed on Apr. 22, 2004.

(51) **Int. Cl.**
A61K 31/44 (2006.01)
A61K 31/56 (2006.01)
A01N 43/42 (2006.01)
A01N 45/00 (2006.01)
A61F 13/00 (2006.01)

(52) **U.S. Cl.** **514/282**; 514/171; 424/422

(58) **Field of Classification Search** 514/282,
514/171; 424/422
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,719,219 A 1/1988 Arvidsson et al.
4,882,335 A 11/1989 Sinclair
5,407,609 A 4/1995 Tice et al.
5,512,593 A 4/1996 Dante
5,654,008 A 8/1997 Herbert et al.
5,792,477 A 8/1998 Rickey et al.
6,143,314 A * 11/2000 Chandrashekar et al. 424/426
6,264,987 B1 7/2001 Wright et al.
6,306,425 B1 10/2001 Tice et al.
6,358,443 B1 3/2002 Herbert et al.
6,495,155 B1 12/2002 Tice et al.
2004/0151774 A1 8/2004 Pauletti et al.

FOREIGN PATENT DOCUMENTS

WO 01/15699 3/2001
WO 01/43726 A 6/2001
WO WO 2004/064752 A2 8/2004
WO WO 2004/108084 A2 12/2004

OTHER PUBLICATIONS

O'Malley, Stephanie S. et al., "Initial and Maintenance Naltrexone Treatment for Alcohol Dependence Using Primary Care vs Specialty Care. A Nested Sequence of 3 Randomized Trials," Arch Intern Med., 163: 1695-1704 (2003).
Latt, Noeline C. et al., "Naltrexone in alcohol dependence: a randomised controlled trial of effectiveness in a standard clinical setting," MJA, 176: 530-534 (2002).
Heinala, Pekka et al., "Targeted Use of Naltrexone Without Prior Detoxification in the Treatment of Alcohol Dependence: A Factorial

Double-Blind, Placebo-Controlled Trial," J Clinical Psychopharmacology, 21(3):287-292 (2001).

"Evidence for the Efficacy of Naltrexone in the Treatment of Alcohol Dependence (Alcoholism)," Addiction Treatment Forum, Ed., Leavitt, Stewart, pp. 1-8 (2002).

Reuning, R.H., et al., "Pharmacokinetic quantitation of naltrexone release from several sustained-released delivery," NIDA, Research Monograph, Institute on Drug Abuse, 28:172-184, (1981).

Yolles, S., et al., "Long acting delivery for narcotic antagonists II: release rates of naltrexone from Poly(lactic acid) composites," PDA J. of Pharm. Sci and Tech., 64(2):348-349, (1995).

Bartus, et al., Vivitrex®, an Injectable, Extended-Release Formulation of Naltrexone, Provides Pharmacokinetic and Pharmacodynamic Evidence of Efficacy for 1 Month in Rats, *Neuropsychopharmacology*, 28:1973-1982 (Aug. 2003).

Comer, Sandra D. et al., "Depot Naltrexone: Long-lasting Antagonism of the Effects of Heroin in Humans," *Psychopharmacology*, 159:351-360 (2002).

Chiang, C.N. et al., "Kinetics of a Naltrexone Sustained-release Preparation," *Clinical Pharmacology and Therapeutics*, 36(5): 704-708.

U.S. Appl. No. 60/554,658, filed Mar. 19, 2004, Elliott Ehrich, et al.

U.S. Appl. No. 60/554,785, filed Mar. 19, 2004, Elliott Ehrich, et al.

U.S. Appl. No. 11/082,420, filed Mar. 17, 2005, Elliott Ehrich, et al.

U.S. Appl. No. 11/082,534, filed Mar. 17, 2005, Elliott Ehrich, et al.

Swift, Robert M., "Drug Therapy for Alcohol Dependence," *New England J. of Med.*, 340(19): 1482-1490 (1999).

Karam-Hage, Maher and Brower, Kirk J., "Gabapentin Treatment for Insomnia Associated With Alcohol Dependence," *Am. J. Psychiatry*, 157(1): 151-153 (2000).

Myrick, M.D., Hugh, et al., "Gabapentin Treatment of Alcohol Withdrawal," *Am. J. of Psychiatry*, 155(11): 1626-1627, (1998).

Malcolm, M.D., Robert, et al., "Update on Anticonvulsants for the Treatment of Alcohol Withdrawal," *Am. J. on Addictions*, 10(1): 16-23, Abstract Only, (2001).

Swift, R., et al., "Naltrexone Effects on Diazepam Intoxication and Pharmacokinetics in Humans," *Psychopharmacology*, 135(3): 256-262 (1998), Abstract Only.

Chaves, M.L., et al., "Diazepam Inhibits Retroactive Interference of Memory in Humans: Pretreatment with Naltrexone Does Not Alter This Effect," *Braz. J. Med. Biol. Res.*, 23(5): 417-421 (1990), Abstract Only.

Fidecka, S. and Langwinski, R., "Effects of Opioid Antagonists on Anticonvulsant and Hypnotic Activity of Benzodiazepines," *Pol. J. Pharmacol.*, 48(4): 409-414 (1996), Abstract Only.

Longo, L.P., et al., "Divalproex Sodium (Depakote) for Alcohol Withdrawal and Relapse Prevention," *J. Addict Dis.*, 21(2): 55-64 (2002), Abstract Only.

Minuk, G.Y., et al., "The Use of Sodium Valproate in the Treatment of Alcoholism," *J. Addict Dis.*, 14(2): 67-74 (1995), Abstract Only.

Reoux, J.P., et al., "Divalproex Sodium in Alcohol Withdrawal: A Randomized Double Blind Placebo-Controlled Clinical Trial," *Alcohol Clin. Exp. Res.*, 25(9): 1324-1329 (2001), Abstract Only.

* cited by examiner

Primary Examiner — Sreeni Padmanabhan

Assistant Examiner — Kendra D Carter

(74) *Attorney, Agent, or Firm* — Elmore Patent Law Group, P.C.; Carolyn S. Elmore; Darlene A. Vanstone

(57) **ABSTRACT**

The inventions described herein arose from unexpected discoveries made during clinical trials with a long acting formulation of naltrexone. As such, the invention includes a method for treating an individual in need of naltrexone comprising the step of parenterally administering a long acting formulation comprising naltrexone and to the use of naltrexone in the manufacture of medicaments for use in such methods.

15 Claims, 4 Drawing Sheets

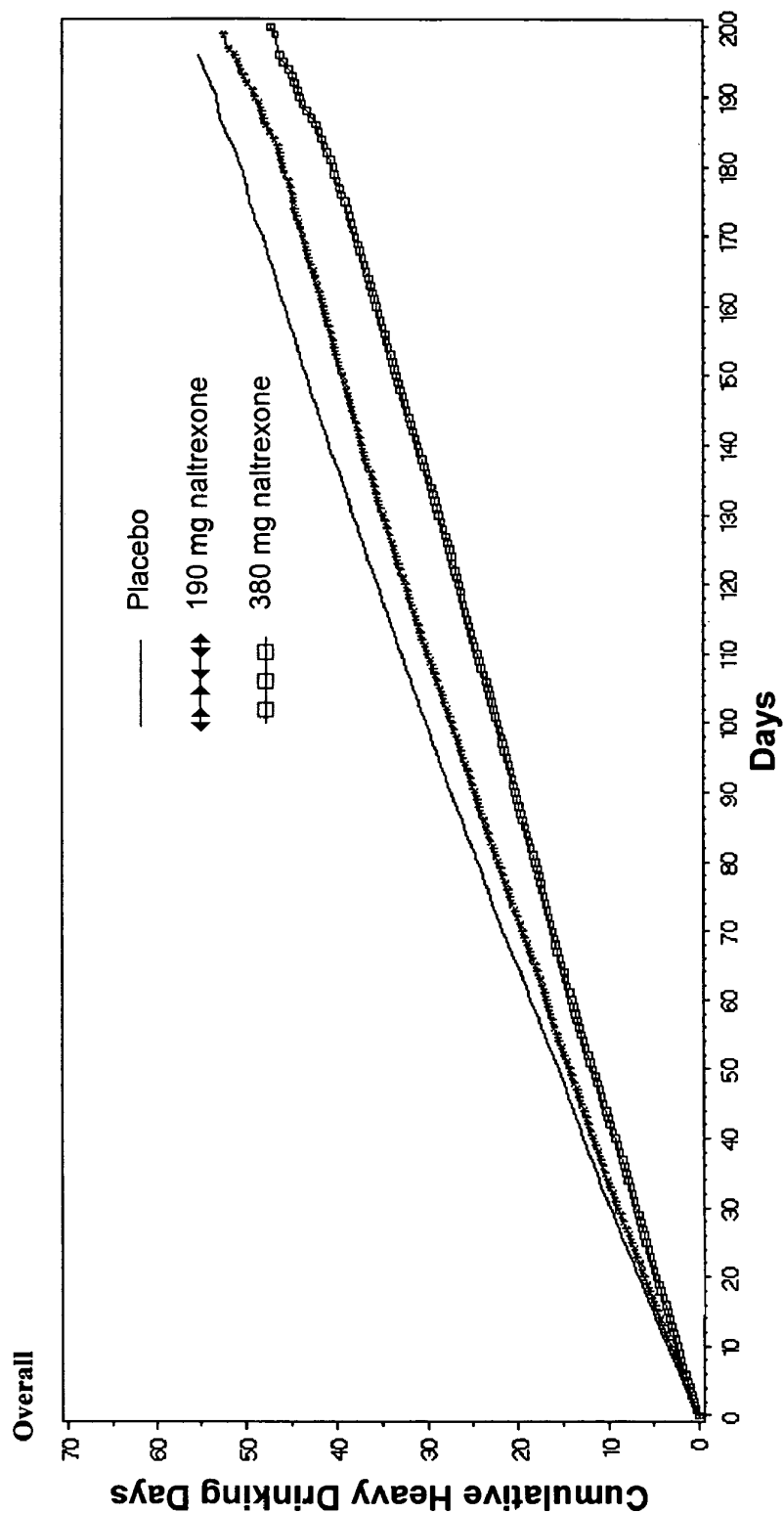


FIG. 1A

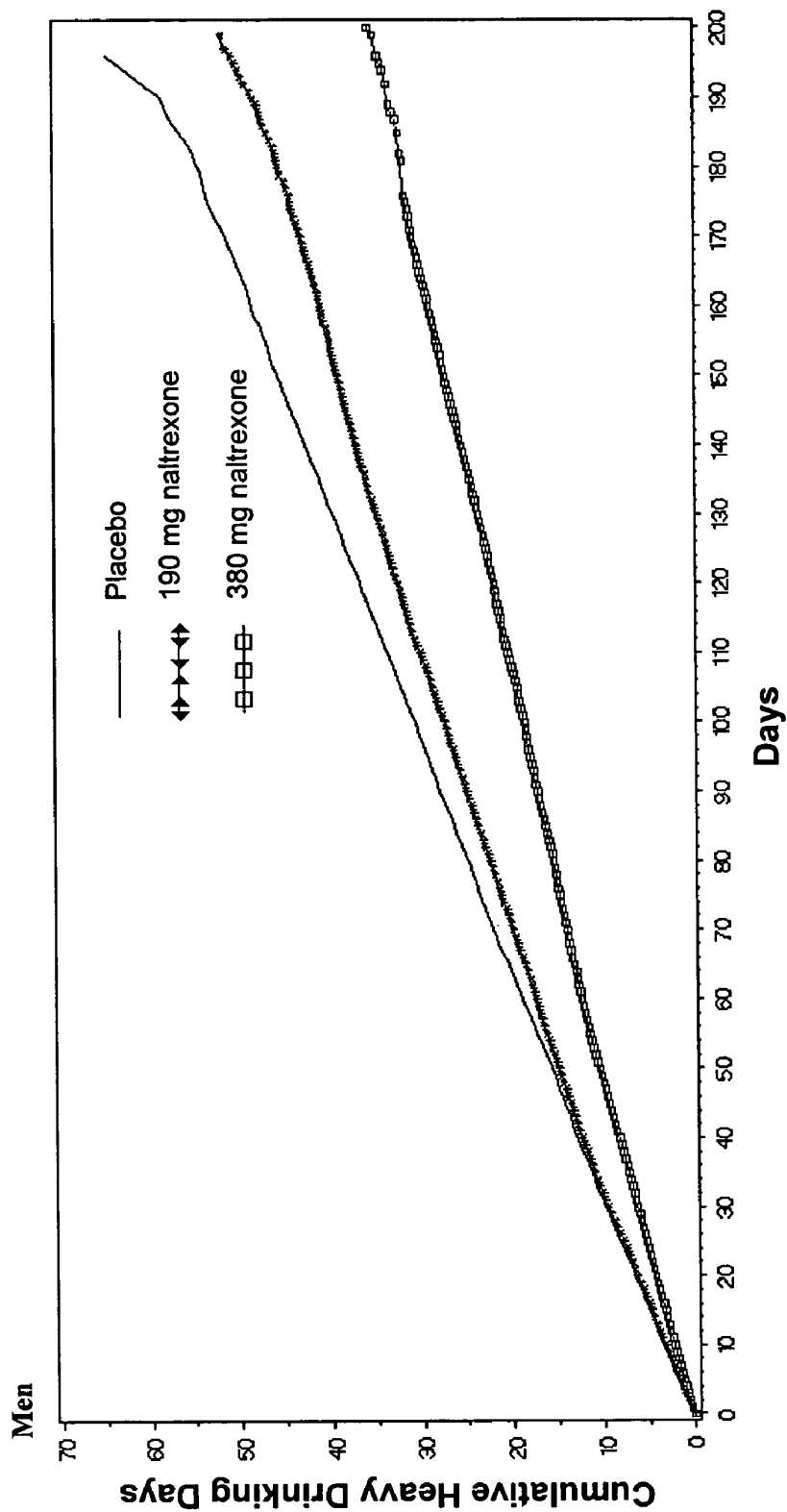


FIG. 1B

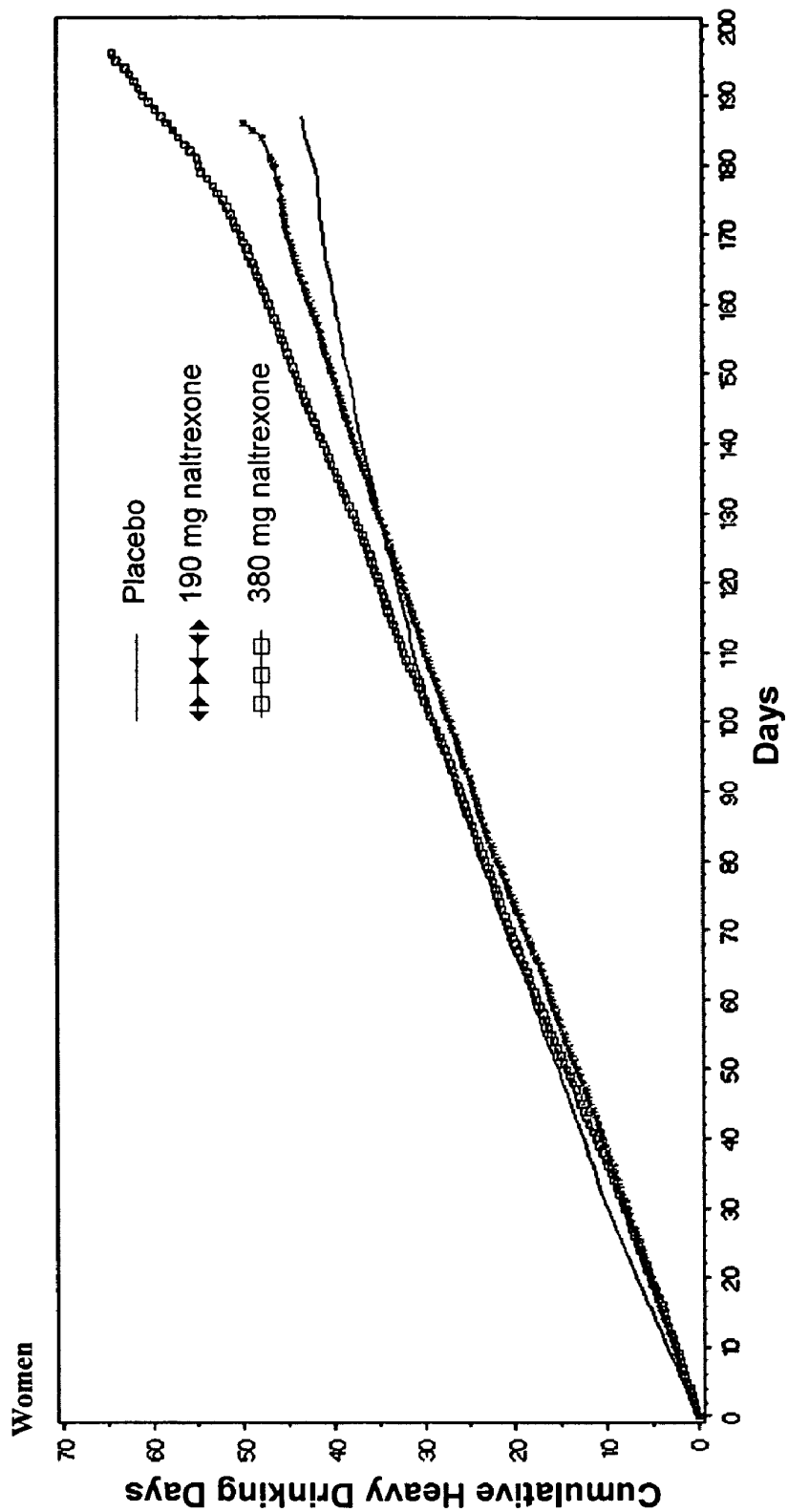


FIG. 1C

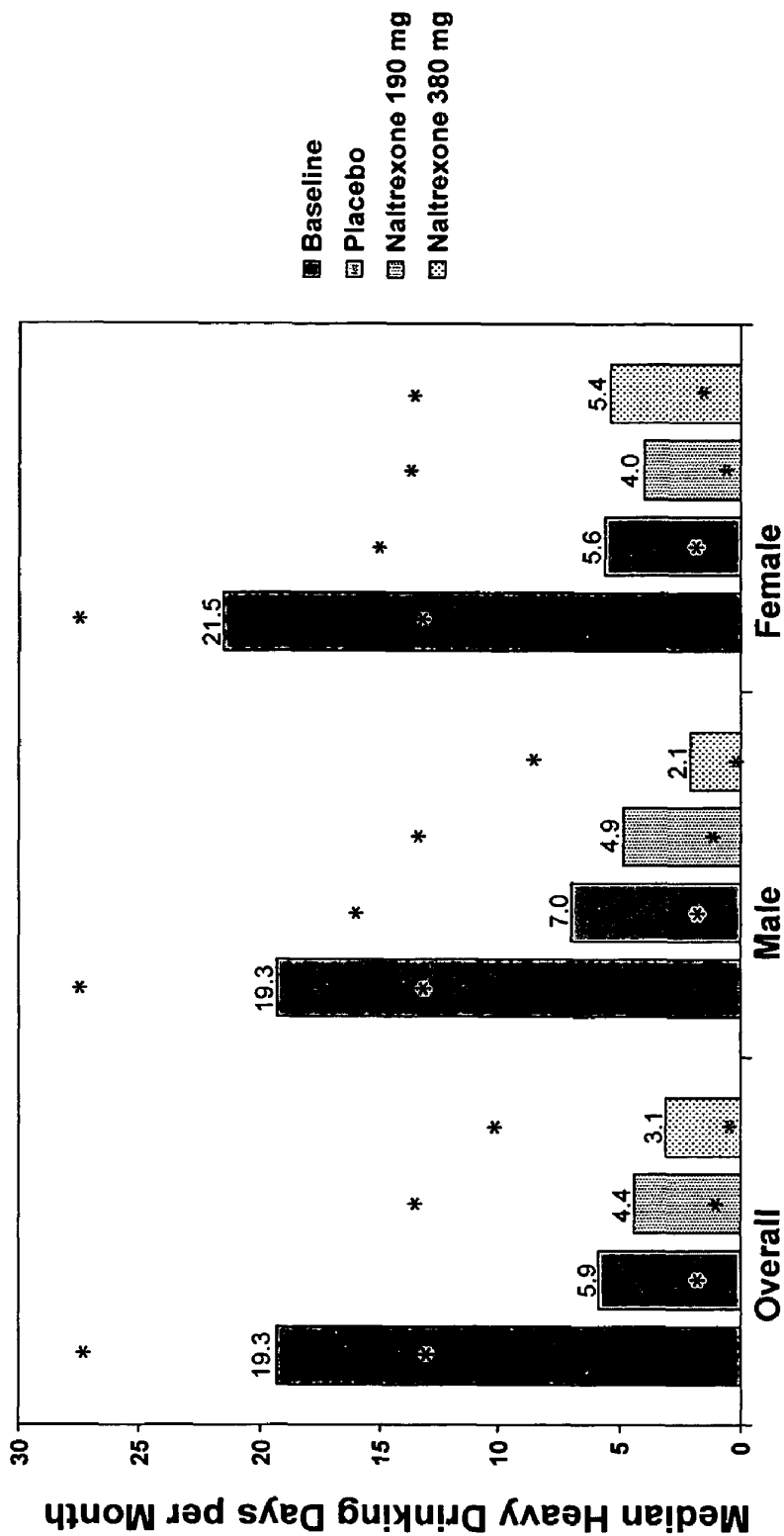


FIG. 2

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.