US008846648B2

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

(10) **Patent No.: US 8,846,648 B2**
(45) **Date of Patent: *Sep. 30, 2014**

(54) **NATURAL COMBINATION HORMONE REPLACEMENT FORMULATIONS AND THERAPIES**

(71) Applicant: **TherapeuticsMD, Inc.**, Boca Raton, FL (US)

(72) Inventors: **Brian A. Bernick**, Boca Raton, FL (US); **Janice Louise Cacace**, Miami, FL (US); **Peter H. R. Persicaner**, Boca Raton, FL (US); **Neda Irani**, Palm Beach Garden, FL (US); **Julia M. Amadio**, Boca Raton, FL (US)

(73) Assignee: **TherapeuticsMD, Inc.**, Boca Raton, FL (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.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **14/099,545**

(22) Filed: **Dec. 6, 2013**

(65) **Prior Publication Data**

US 2014/0088051 A1 Mar. 27, 2014

Related U.S. Application Data

(62) Division of application No. 13/684,002, filed on Nov. 21, 2012, now Pat. No. 8,633,178.

(60) Provisional application No. 61/662,265, filed on Jun. 20, 2012, provisional application No. 61/661,302, filed on Jun. 18, 2012, provisional application No. 61/563,408, filed on Nov. 23, 2011.

(51) **Int. Cl.**

A01N 45/00	(2006.01)
A61K 9/48	(2006.01)
A61K 31/565	(2006.01)
A61K 9/16	(2006.01)
A61K 31/57	(2006.01)

(52) **U.S. Cl.**

CPC ***A61K 31/57*** (2013.01); ***A61K 9/4858*** (2013.01); ***A61K 31/565*** (2013.01); ***A61K 9/16*** (2013.01)

USPC **514/169**; 424/452

(58) **Field of Classification Search**

USPC 514/169

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

1,967,351	A	7/1934	Doisy
2,379,832	A	7/1945	Serini et al.
2,649,399	A	8/1953	Grant et al.
3,198,707	A	8/1965	Nomaine et al.
3,478,070	A	11/1969	Smith et al.
3,526,648	A	9/1970	Bertin et al.
3,710,795	A	1/1973	Higuchi et al.
3,729,560	A	4/1973	Hagerman
3,729,566	A	4/1973	Ericsson et al.
3,755,573	A	8/1973	Berman
3,755,575	A	8/1973	Lerner
3,903,880	A	9/1975	Higuchi et al.
3,916,898	A	11/1975	Robinson
3,916,899	A	11/1975	Higuchi et al.
3,921,636	A	11/1975	Zaffaroni
3,923,997	A	12/1975	Meuly
3,948,254	A	4/1976	Zaffaroni
3,971,367	A	7/1976	Zaffaroni
3,977,404	A	8/1976	Theeuwes
3,993,072	A	11/1976	Zaffaroni
4,008,719	A	2/1977	Theeuwes
4,012,496	A	3/1977	Hartmann et al.
4,014,334	A	3/1977	Theeuwes et al.
4,014,987	A	3/1977	Heller et al.
4,016,251	A	4/1977	Higuchi et al.
4,071,623	A	1/1978	Van Der Vies
4,093,709	A	6/1978	Choi
4,154,820	A	5/1979	Simoons
4,155,991	A	5/1979	Schopflin et al.
4,196,188	A	4/1980	Besins
4,215,691	A	8/1980	Wong
4,237,885	A	12/1980	Wong
4,310,510	A	1/1982	Sherman et al.
4,327,725	A	5/1982	Cortese et al.
4,372,951	A	2/1983	Vorys
4,384,096	A	5/1983	Sonnabend

(Continued)

FOREIGN PATENT DOCUMENTS

CN	102258455	A	11/2011
EP	0275716	A1	7/1988
EP	0622075	A1	11/1994
EP	0785211	A1	1/1996
EP	0811381	A1	6/1997

(Continued)

OTHER PUBLICATIONS

Chempro, "Fatty Acid Composition of Some Major Oils," available at http://www.chempro.in/fattyacid.htm, webpage captured on May 26, 2010 (2 total pages).*

(Continued)

Primary Examiner — Frederick Krass
Assistant Examiner — Dennis J Parad
(74) *Attorney, Agent, or Firm* — Kilpatrick Townsend & Stockton LLP; Marian D. Walker

(57) **ABSTRACT**

Estrogen and progesterone replacement therapies are provided herein. Among others, the following formulations are provided herein: solubilized estradiol without progesterone; micronized progesterone without estradiol; micronized progesterone with partially solubilized progesterone; solubilized estradiol with micronized progesterone; solubilized estradiol with micronized progesterone in combination with partially solubilized progesterone; and solubilized estradiol with solubilized progesterone.

20 Claims, 4 Drawing Sheets