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

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

(58) **Field of Classification Search**

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See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2,232,438	A		2/1941	Butenandt
4,900,734	A	*	2/1990	Maxson et al. 514/171
5,538,736	A		7/1996	Barth et al.
5,556,635	A		9/1996	Grognet et al.
5,580,572	A		12/1996	Liorzou et al.
5,605,702	A		2/1997	Math et al.
5,607,691	A		3/1997	Solas et al.
5,607,693	A		3/1997	Bonte et al.
5,609,617	A		3/1997	Cady et al.
5,626,866	A		5/1997	Heiber et al.
5,653,983	A		8/1997	Bonte et al.
5,660,839	A		8/1997	Allec et al.
5,662,927	A		9/1997	Ehrlich et al.
5,663,160	A		9/1997	Dumas et al.
5,686,097	A		11/1997	Crisologo et al.
5,693,335	A		12/1997	Xia et al.
5,700,480	A		12/1997	Hille et al.
5,719,197	A		2/1998	Mantelle et al.
5,770,220	A		6/1998	Meconi et al.
5,770,227	A		6/1998	Dong et al.
5,780,044	A		7/1998	Tipton et al.
5,780,050	A		7/1998	Jain et al.
5,788,984	A		8/1998	Schmidt et al.
5,820,878	A		10/1998	Shinmura et al.
5,840,327	A		11/1998	Gale et al.
5,843,468	A		12/1998	Yum et al.
5,843,979	A		12/1998	Wille et al.
5,858,394	A		1/1999	Lipp et al.
5,863,552	A		1/1999	Yue

(Continued)

FOREIGN PATENT DOCUMENTS

WO	WO9619975	7/1996
WO	WO0241878	5/2002

(Continued)

OTHER PUBLICATIONS

Abitec Corporation, Excipients for the Pharmaceutical Industry—Regulatory and Product Information, 2013, 2 pages.

(Continued)

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(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.

18 Claims, 4 Drawing Sheets