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

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(58) **Field of Classification Search**

USPC 514/169; 424/452

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2,232,438	A	2/1941	Butenandt
5,538,736	A	7/1996	Hoffmann et al.
5,556,635	A	9/1996	Istin et al.
5,580,572	A	12/1996	Mikler et al.
5,605,702	A	2/1997	Teillaud et al.
5,607,691	A	3/1997	Hale et al.
5,607,693	A	3/1997	Bonte et al.
5,609,617	A	3/1997	Shealy et al.
5,626,866	A	5/1997	Ebert et al.
5,653,983	A	8/1997	Meybeck 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	Meybeck et al.
5,686,097	A	11/1997	Taskovich 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	Kanios 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	Yewey et al.
5,780,050	A	7/1998	Jain et al.
5,788,984	A	8/1998	Guenther et al.
5,820,878	A	10/1998	Hirano et al.
5,840,327	A	11/1998	Gale et al.
5,843,468	A	12/1998	Burkoth 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
5,882,676	A	3/1999	Lee et al.
5,885,612	A	3/1999	Meconi et al.
5,888,533	A	3/1999	Dunn
5,891,462	A	4/1999	Carrara

(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.

Corbett et al., "Trends in Pharmacy Compounding for Women's Health in North Carolina: Focus on Vulvodynia," Southern Medical Journal, vol. 107, No. 7, Jul. 2014, pp. 433-436.

Shrier et al., "Mucosal Immunity of the Adolescent Female Genital Tract," Journal of Adolescent Health, 2003; 32:183-186.

Gattefossé SAS, Material Safety Data Sheet, Gelot 64, 2012, 8 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.

15 Claims, 4 Drawing Sheets