ESTROGEN RECEPTOR MODULATOR AND USES THEREOF

RELATED APPLICATIONS

[0001] This application claims the benefit of U.S provisional patent application no. 61/836,901 entitled "ESTROGEN RECEPTOR MODULATOR AND USES THEREOF" filed on June 19, 2013; and U.S provisional patent application no. 61/952,430 entitled "ESTROGEN RECEPTOR MODULATOR AND USES THEREOF" filed on March 13, 2014; all of which are incorporated by reference in their entirety.

FIELD OF THE INVENTION

[0002] Described herein are compounds, including pharmaceutically acceptable salts, solvates, metabolites, prodrugs thereof, methods of making such compounds, pharmaceutical compositions comprising such compounds, and methods of using such compounds to treat, prevent or diagnose diseases or conditions that are estrogen sensitive, estrogen receptor dependent or estrogen receptor mediated.

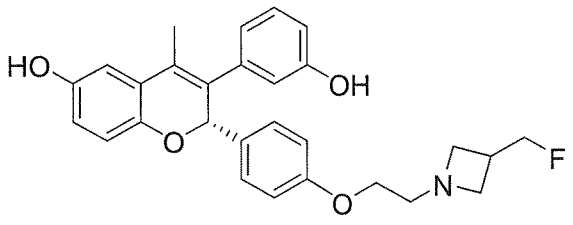
BACKGROUND OF THE INVENTION

[0003] The estrogen receptor ("ER") is a ligand-activated transcriptional regulatory protein that mediates induction of a variety of biological effects through its interaction with endogenous estrogens. Endogenous estrogens include 17β-estradiol and estrones. ER has been found to have two isoforms, ER-α and ER-β.

[0004] Estrogens and estrogen receptors are implicated in a number of diseases or conditions, such as breast cancer, lung cancer, ovarian cancer, colon cancer, prostate cancer, endometrial cancer, uterine cancer, as well as others diseases or conditions.

SUMMARY

[0004a] In one aspect, there is provided a compound that has the following structure of Formula (III):



Formula (III)

or a pharmaceutically acceptable salt thereof.

[0004b] In another aspect, there is provided a pharmaceutically acceptable salt of the compound as described herein.

[0004c] In another aspect, there is provided a pharmaceutical composition comprising a compound or a pharmaceutically acceptable salt as described herein.

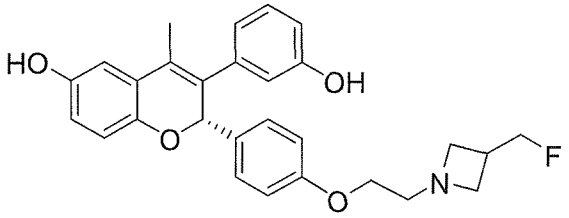
[0004d] In another aspect, there is provided a compound, or a pharmaceutically acceptable salt thereof, as described herein for use as a medicament.

[0004e] In another aspect, there is provided use of a compound, or a pharmaceutically acceptable salt thereof, as described herein in the manufacture of a medicament for the treatment of breast cancer in a mammal.

[0005] Presented herein are compounds of Formula (I), (II), and (III), or a pharmaceutically acceptable salt, solvate or prodrug thereof, that diminish the effects of estrogens with estrogen receptors and/or lower the the concentrations of estrogen receptors, and therefore, are useful as agents for the treatment or prevention of diseases or conditions in which

WHAT IS CLAIMED IS:

1. A compound that has the following structure of Formula (III):



Formula (III)

or a pharmaceutically acceptable salt thereof.

2. A pharmaceutically acceptable salt of the compound of claim 1.

3. The pharmaceutically acceptable salt of claim 2, wherein the pharmaceutically acceptable salt of the compound is an acid addition salt.

4. The pharmaceutically acceptable salt of claim 2, wherein the pharmaceutically acceptable salt of the compound is a hydrochloric acid salt, a hydrobromic acid salt, a sulfuric acid salt, a phosphoric acid salt, a metaphosphoric acid salt, an acetic acid salt, a propionic acid salt, a hexanoic acid salt, a cyclopentanepropionic acid salt, a glycolic acid salt, a pyruvic acid salt, a lactic acid salt, a malonic acid salt, a succinic acid salt, a malic acid salt, a L-malic acid salt, a maleic acid salt, an oxalic acid salt, a fumaric acid salt, a trifluoroacetic acid salt, a tartaric acid salt, a L-tartaric acid salt, a citric acid salt, a benzoic acid salt, a 3-(4-hydroxybenzoyl)benzoic acid salt, a cinnamic acid salt, a mandelic acid salt, a methanesulfonic acid salt, an ethanesulfonic acid salt, a 1,2-ethanedisulfonic acid salt, a 2-hydroxyethanesulfonic acid salt, a benzenesulfonic acid salt, a toluenesulfonic acid salt, a 2-naphthalenesulfonic acid salt, a 4-methylbicyclo-[2.2.2]oct-2-ene-1-carboxylic acid salt, a glucoheptonic acid salt, a 4,4'-methylenebis-(3-hydroxy-2-ene-1-carboxylic acid) salt, a 3-phenylpropionic acid salt, a trimethylacetic acid salt, a tertiary butylacetic acid salt, a lauryl sulfuric acid salt, a gluconic acid salt, a glutamic acid salt, a hydroxynaphthoic acid salt, a salicylic acid salt, a stearic acid salt, a muconic acid salt, a butyric acid salt, a phenylacetic acid salt, a phenylbutyric acid salt, or a valproic acid salt.

5. The pharmaceutically acceptable salt of claim 2, wherein the pharmaceutically acceptable salt of the compound is a hydrochloric acid salt.

6. A pharmaceutical composition comprising a compound or a pharmaceutically acceptable salt as claimed in any one of claims 1 to 5.

7. The pharmaceutical composition of claim 6, wherein the pharmaceutical composition is formulated for intravenous injection, subcutaneous injection, oral administration, or topical administration.

8. The pharmaceutical composition of claim 6, wherein the pharmaceutical composition is a tablet, a pill, a capsule, a liquid, a suspension, a gel, a dispersion, a solution, an emulsion, an ointment, or a lotion.

9. A compound, or a pharmaceutically acceptable salt thereof, of any one of claims 1-5 for use as a medicament.

10. Use of a compound, or a pharmaceutically acceptable salt thereof, of any one of claims 1-5 in the manufacture of a medicament for the treatment of breast cancer in a mammal.

11. The use of claim 10 in combination with an analysis of CA-125 levels in a blood sample from the mammal.