
, or a pharmaceutically acceptable salt thereof.

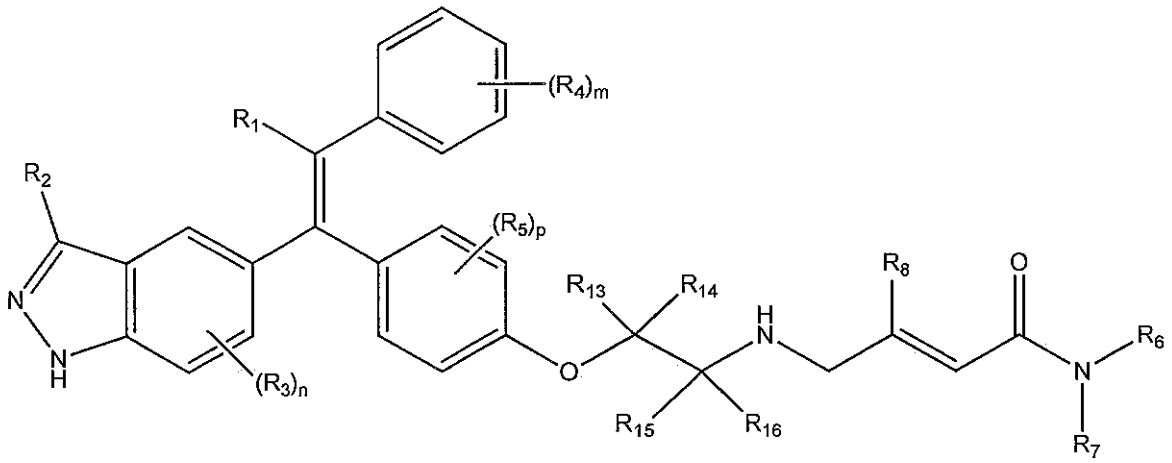
A further example may provide a method of treating breast cancer comprising administering to a subject a compound according to any one of the preceding paragraphs. In one aspect, the present invention is directed to pharmaceutical composition comprising a compound or pharmaceutically acceptable salt according to the present invention for use in treating breast cancer. The breast cancer may be an ER-positive breast cancer. The subject may express a mutant ER-α protein. An embodiment may provide use of a compound as in the paragraphs above for treating breast cancer. In some embodiments the breast cancer is an ER-positive breast cancer. In some embodiments said subject expresses a mutant ER-α protein. In some embodiments a compound as presented above is used in the preparation of a medicament for treatment of breast cancer.

In embodiments, the compounds disclosed herein are useful for inhibiting the cell culture growth of MCF7 ER-alpha (wildtype) and MCF7 ER-alpha (Y537S mutant) cells. Other compounds (e.g., tamoxifen, raloxifene and fulvestrant) known to inhibit the cell culture growth of MCF7 ER-alpha (wildtype) cells are currently used to treat breast cancer in human patients. Hence, the compounds disclosed herein are useful for treating ER-alpha expressing breast cancer in human patients, and are useful for treating Y537S mutant ER-alpha expressing breast cancer in human patients.

In embodiments, the compounds disclosed herein are useful for treating breast cancer. In embodiments, the breast cancer is ER-α+. In embodiments, the breast cancer expresses an ER-α mutation, which is L536Q (Robinson *et al. Nat Genet.* 2013 Dec;45(12)), L536R (Toy *et al. Nat Genet.* 2013 Dec;45(12):1439-45), Y537S (Toy *et al. Nat Genet.* 2013 Dec;45(12):1439-45; Robinson *et al. Nat Genet.* 2013 Dec;45(12); Jeselsohn *et al. Clin Cancer Res.* 2014 Apr 1;20(7):1757-67), Y537N (Toy *et al. Nat Genet.* 2013 Dec;45(12):1439-45; Jeselsohn *et al. Clin Cancer Res.* 2014 Apr 1;20(7):1757-67), Y537C (Toy *et al. Nat Genet.* 2013 Dec;45(12):1439-45; Jeselsohn *et al. Clin Cancer Res.* 2014 Apr 1;20(7):1757-67) and D538G (Toy *et al. Nat Genet.* 2013 Dec;45(12):1439-45; Robinson *et al. Nat Genet.* 2013 Dec;45(12); Jeselsohn *et al. Clin Cancer Res.* 2014 Apr 1;20(7):1757-67; Merenbakh-Lamin *et al. Cancer Res.* 2013 Dec 1;73(23):6856-64); and Yu et al., (2014)

WHAT IS CLAIMED IS:

1. A compound given by formula II:



II

wherein:

R_1 is selected from the group consisting of methyl, ethyl, cyclobutyl, cyclopropyl, propyl, isopropyl, $-CH_2CF_3$, $-CH_2CH_2F$, and $-CH_2CH_2Cl$;

R_2 is selected from the group consisting of H and F;

n is 0-1;

R_3 is F when n=1;

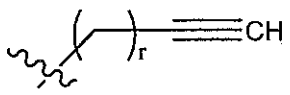
m is 0-2;

R_4 are the same or different and are independently selected from the group consisting of F, CF_3, Cl, isopropyl, $-OCH_3$, $-OCHF_2$, $-OCF_3$, ethyl and methyl;

p is 0-1;

R_5 is F when p=1;

R_6 and R_7 are the same or different and are independently selected from the group consisting of methyl, ethyl, propyl, $-CH_2CH_2OH$ and



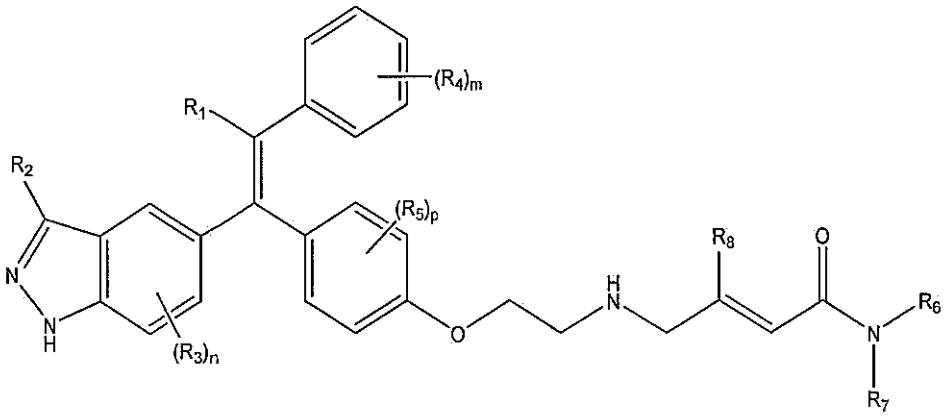
, wherein r is 1 or 2; or, wherein R_6 and R_7 form a 4-6 membered heterocyclic ring with the N to which they are attached, wherein said heterocyclic ring optionally includes an oxygen atom, and wherein said heterocyclic ring is optionally substituted with F, or $-CH_2F$;

R_8 is selected from the group consisting of H and $-CH_3$;

and R_{13}, R_{14}, R_{15}, and R_{16} are independently selected from the group consisting of –H or $–CH_3$;

or a pharmaceutically acceptable salt thereof.

2. The compound or pharmaceutically acceptable salt of claim 1, given by formula I:



I

wherein:

R_1 is selected from the group consisting of methyl, ethyl, cyclobutyl, cyclopropyl and $-CH_2CH_2Cl$;

R_2 is selected from the group consisting of H and F;

n is 0-1;

R_3 is F when n=1;

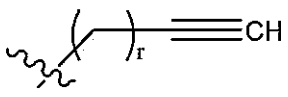
m is 0-2;

R_4 are the same or different and are independently selected from the group consisting of F, CF_3, Cl, isopropyl, $-OCH_3$, $-OCHF_2$, $-OCF_3$, ethyl and methyl;

p is 0-1;

R_5 is F when p=1;

R_6 and R_7 are the same or different and are independently selected from the group consisting of methyl, ethyl, propyl, $-CH_2CH_2OH$ and



, wherein r is 1 or 2;

or, wherein R_6 and R_7 form a 4-6 membered heterocyclic ring with the N to which they are attached, wherein said heterocyclic ring optionally includes an oxygen atom, and wherein said heterocyclic ring is optionally substituted with F, or $–CH_2F$;

R_8 is selected from the group consisting of H and CH_3;

or a pharmaceutically acceptable salt thereof.

3. The compound or pharmaceutically acceptable salt thereof according to claim 2, wherein R_1 is ethyl.

4. The compound or pharmaceutically acceptable salt thereof according to claim 2, wherein R_1 is cyclobutyl.

5. The compound or pharmaceutically acceptable salt thereof as in any one of the preceding claims, wherein R_6 and R_7 are both methyl.

6. The compound or pharmaceutically acceptable salt thereof as in any one of the preceding claims, wherein R_8 is H.

7. The compound or pharmaceutically acceptable salt thereof as in any one of the preceding claims, wherein R_2 is F.

8. The compound or pharmaceutically acceptable salt thereof as in one of claims 1-6, wherein R_2 is H.

9. The compound or pharmaceutically acceptable salt thereof as in one of claims 1-6, wherein m is 2, and one of R_4 is F and the other R_4 is Cl.

10. The compound or pharmaceutically acceptable salt thereof as in one of claims 1-6, wherein m is 2 and both of R_4 are F.

11. The compound or pharmaceutically acceptable salt thereof as in one of claims 1-6, wherein m is 0.

12. The compound or pharmaceutically acceptable salt thereof as in one of claims 1-6, wherein n is 1 and R_3 is F.

13. The compound or pharmaceutically acceptable salt thereof as in one of claims 1-6, wherein n is 0.

14. The compound or pharmaceutically acceptable salt thereof as in one of claims 1-6, wherein p is 1 and R_5 is F.

15. The compound or pharmaceutically acceptable salt thereof as in one of claims 1-6, wherein p is 0.

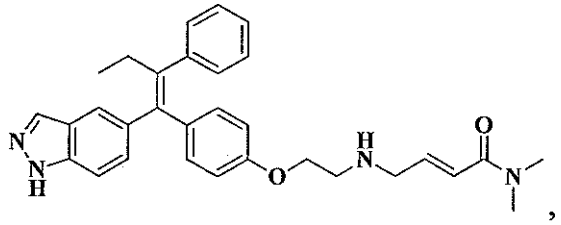
16. A compound selected from the group consisting of (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-phenylbut-1-en- 1-yl)phenoxy) ethyl) amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(3-fluoro-1*H*-indazol-5-yl)-2-phenyl but-1-en-1-yl) phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(3-fluoro-1*H*-indazol-5-yl)-2-(3-fluoro-5-(trifluoromethyl) phenyl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(4-fluoro-1*H*-indazol-5-yl)-2-phenyl but-1-en-1-yl) phenoxy) ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-2-(3,5-difluorophenyl)-1-(1*H*-indazol-5-yl)but-1-en-1-yl) phenoxy)ethyl)amino)-N,N-dimethylbut-2-enamide; (E)-4-((2-(4-((E)-2-(3,4-difluorophenyl)-1-(1*H*-indazol-5- yl)but-1-en-1-yl) phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-2-(3-chloro-5-fluorophenyl)-1-(1*H*-indazol-5-yl)but-1-en-1-yl) phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-phenylbut-1-en-1- yl)phenoxy) ethyl) amino)-*N*-methyl-*N*-(prop-2-yn-1-yl)but-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)phenoxy)ethyl) amino)-*N*-(but-3-yn-1-yl)-*N*-methylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)phenoxy)ethyl) amino)-1-(azetidin-1-yl)but-2-en-1-one; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-phenylbut-1-en-1- yl)phenoxy)ethyl) amino)-1-(pyrrolidin-1-yl)but-2-en-1-one; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)phenoxy)ethyl) amino)-1-(piperidin-1-yl)but-2-en-1-one; (*E*)-4-((2-(4-((*E*)-2-cyclobutyl-1-(1*H*-indazol-5-yl)-2- phenylvinyl)phenoxy) ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-2-cyclobutyl-1-(3-fluoro-1*H*-indazol-5- yl)-2-phenylvinyl) phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide 2,2,2-trifluoro acetate; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-phenylbut-1-en-1- yl)phenoxy)ethyl) amino)-1-morpholinobut-2-en-1-one; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-phenylbut-1-en- 1-yl)phenoxy)ethyl) amino)-*N*-ethyl-*N*-methylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-phenylbut-1-en- 1-yl)phenoxy)ethyl) amino)-*N*-methyl-*N*-propylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)phenoxy)ethyl)amino)-*N*-(2-hydroxyethyl)-*N*-methylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-2-(2-chloro-4-fluorophenyl)-1-(3- fluoro-1*H*-indazol-5-yl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-

2-phenylbut-1-en-1- yl)phenoxy)ethyl) amino)-*N,N*,3-trimethylbut-2-enamide; (*Z*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)phenoxy)ethyl) amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-2-cyclobutyl-1-(1*H*-indazol-5-yl)-2- phenylvinyl)phenoxy) ethyl)amino)-1-morpholinobut-2-en-1-one; (*E*)-4-((2-(4-((*E*)-2-cyclobutyl-1-(4-fluoro-1*H*-indazol-5- yl)-2-phenylvinyl) phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-((5-((*Z*)-1-(1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)pyridin-2-yl) oxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-(o-tolyl)but-1-en- 1-yl)phenoxy) ethyl)amino)-*N*-(2-hydroxyethyl)-*N*-methylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-2-(2-chloro-4-fluorophenyl)-1-(3- fluoro-1*H*-indazol-5-yl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N*-(2-hydroxyethyl)-*N*-methylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-(4-isopropyl phenyl)but-1-en-1-yl) phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-4-chloro-1-(1*H*-indazol-5-yl)-2-phenyl but-1-en-1-yl)phenoxy) ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-(4-isopropyl phenyl)but-1-en-1-yl) phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-2-(2-(difluoromethoxy)phenyl)-1-(1*H*- indazol-5-yl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-(2-(trifluoro-methoxy)phenyl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-(2-isopropyl phenyl)but-1-en-1-yl) phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-2-(2-ethylphenyl)-1-(1*H*-indazol-5-yl) but-1-en-1-yl)phenoxy) ethyl)amino)-N,N-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-(o-tolyl)but-1- en-1-yl)phenoxy)ethyl) amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-((5-((*Z*)-1-(1*H*-indazol-5-yl)-2-phenylbut-1- en-1-yl)pyrimidin-2-yl) oxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-1-(azetidin-1-yl)-4-((2-(4-((*E*)-2-cyclobutyl-1-(1*H*- indazol-5-yl)-2-phenylvinyl) phenoxy)ethyl)amino)but-2-en-1-one; (*E*)-1-(azetidin-1-yl)-4-((2-(4-((*E*)-2-cyclobutyl-1-(3- fluoro-1*H*-indazol-5-yl)-2-phenylvinyl)phenoxy)ethyl)amino)but-2-en-1-one; (*E*)-4-((2-(4-((*E*)-2-cyclobutyl-1-(1*H*-indazol-5-yl)-2- phenylvinyl) phenoxy) ethyl)amino)-*N*-(2-hydroxyethyl)-*N*-methylbut-2-enamide; (*E*)-1-(azetidin-1-yl)-4-((2-(4-((*E*)-2-cyclobutyl-1-(1*H*- indazol-5-yl)-2-(o-tolyl) vinyl)phenoxy)ethyl)amino)but-2-en-1-one; (*E*)-4-((2-(4-((*E*)-1-(3-fluoro-1*H*-indazol-5-yl)-2-(2-fluoro phenyl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(3-fluoro-1*H*-indazol-5-yl)-2-(3-fluoro phenyl)but-1-en-1-yl) phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(3-fluoro-1*H*-indazol-5-yl)-2-(3- fluorophenyl)but-1-en-1-yl) phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-2-(2-chloro-4-fluorophenyl)-2- cyclobutyl-1-(3-fluoro-1*H*-indazol-5-yl)vinyl)phenoxy)ethyl)amino)-*N,N*-

dimethylbut-2-enamide; (*E*)-4-((2-(2-fluoro-4-((*Z*)-1-(3-fluoro-1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-2-(2,6-difluorophenyl)-1-(3-fluoro-1*H*-indazol-5-yl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(3-fluoro-1*H*-indazol-5-yl)-2-(pyridin-3-yl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(3-fluoro-1*H*-indazol-5-yl)-2-(pyridin-4-yl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-phenylprop-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-2-cyclopropyl-1-(1*H*-indazol-5-yl)-2-phenylvinyl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-2-(2-chloro-4-fluorophenyl)-1-(4-fluoro-1*H*-indazol-5-yl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-((5-((*Z*)-2-(2-chloro-4-fluorophenyl)-1-(3-fluoro-1*H*-indazol-5-yl)but-1-en-1-yl)pyridin-2-yl)oxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-((5-((*Z*)-2-(2-chloro-4-fluorophenyl)-4,4,4- trifluoro-1-(3-fluoro-1*H*-indazol-5-yl)but-1-en-1-yl)pyridin-2-yl)oxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-*N,N*-dimethyl-4-((2-((5-((*Z*)-4,4,4-trifluoro-1- (3-fluoro-1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)pyridin-2-yl)oxy)ethyl)amino)but-2-enamide; (*E*)-*N,N*-dimethyl-4-((2-(4-((*E*)-4,4,4-trifluoro-1-(3- fluoro-1*H*-indazol-5-yl)-2-(3-fluoropyridin-4-yl)but-1-en-1-yl)phenoxy)ethyl)amino)but-2-enamide; (*E*)-*N,N*-dimethyl-4-((2-((5-((*Z*)-4,4,4-trifluoro-1-(3-fluoro-1H-indazol-5-yl)-2-(3-fluoropyridin-4-yl)but-1-en-1-yl)pyridin-2-yl)oxy)ethyl)amino)but-2-enamide; (*E*)-*N,N*-dimethyl-4-((2-(4-((*E*)-2-phenyl-1-(1*H*-pyrazolo[4,3-b]pyridin-5-yl)but-1-en-1-yl)phenoxy)ethyl)amino)but-2-enamide; (*E*)-4-((2-(3-fluoro-4-((*Z*)-1-(3-fluoro-1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-2-(2,4-difluorophenyl)-1-(3-fluoro-1*H*-indazol-5-yl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(3,6-difluoro-1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(3-fluoro-1*H*-indazol-5-yl)-2-(pyridin-2-yl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-((5-((*Z*)-1-(3-fluoro-1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)pyridin-2-yl)oxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-*N,N*-dimethyl-4-((2-(4-((*E*)-4,4,4-trifluoro-1-(3-fluoro-1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)phenoxy)ethyl)amino)but-2-enamide; (*E*)-4-((2-((5-((*Z*)-2-cyclobutyl-1-(3-fluoro-1*H*-indazol-5-yl)-2-phenylvinyl)pyridin-2-yl)oxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-2-(2-chlorophenyl)-1-(3-fluoro-1*H*-indazol-5-yl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-2-(2-chloro-4-fluorophenyl)-1-(1*H*-indazol-5-yl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-

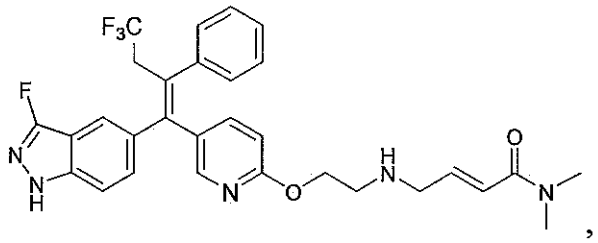
enamide; (*E*)-4-((2-(4-((*E*)-1-(3-fluoro-1*H*-indazol-5-yl)-2-(pyridin-4-yl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N*-(2-hydroxyethyl)-*N*-methylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(7-fluoro-1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(3-fluoro-1*H*-indazol-5-yl)-2-phenylpent-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(3,7-difluoro-1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-2-(2,5-difluorophenyl)-1-(3-fluoro-1*H*-indazol-5-yl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(3-fluoro-1*H*-indazol-5-yl)-2-(3-fluoropyridin-4-yl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(3-fluoro-1*H*-indazol-5-yl)-3-methyl-2-phenylbut-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-5-((2-(4-((*E*)-4-fluoro-1-(3-fluoro-1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylpent-2-enamide; (*E*)-5-((2-(4-((*E*)-2-(2-chloro-4-fluorophenyl)-1-(3-fluoro-1*H*-indazol-5-yl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylpent-2-enamide; (*E*)-4-((2-(4-((*E*)-2-(2-chloro-4-fluorophenyl)-1-(3-fluoro-1*H*-indazol-5-yl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*,2-trimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-2-(2-chloro-4-fluorophenyl)-4,4,4-trifluoro-1-(3-fluoro-1*H*-indazol-5-yl)but-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-(phenyl-d5)but-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)phenoxy)ethyl)amino)-*N,N*-dimethylpent-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)phenoxy)propyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((1-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)phenoxy)propan-2-yl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-((6-((*Z*)-1-(3-fluoro-1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)pyridin-3-yl)oxy)ethyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((3-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)phenoxy)propyl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((3-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)phenoxy)butan-2-yl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((1-(4-((*E*)-1-(1*H*-indazol-5-yl)-2-phenylbut-1-en-1-yl)phenoxy)-2-methylpropan-2-yl)amino)-*N,N*-dimethylbut-2-enamide; (*E*)-4-((2-(4-((*E*)-1-(1H-indazol-5-yl)-2-phenylbut-1-en-1-yl)phenoxy)-2-methylpropyl)amino)-*N,N*-dimethylbut-2-enamide; and (*E*)-4-((2-(4-((*E*)-2-cyclobutyl-1-(3-fluoro-1*H*-indazol-5-yl)-2-phenylvinyl)phenoxy)ethyl)amino)-*N*-(2-hydroxyethyl)-*N*-methylbut-2-enamide; or a pharmaceutically acceptable salt thereof.

17. A compound having the following formula:



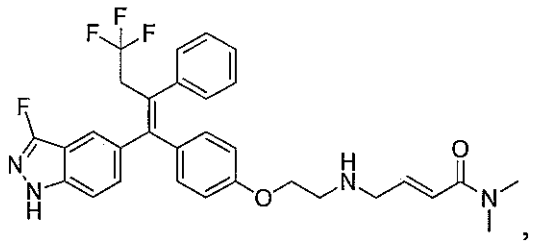
or a pharmaceutically acceptable salt thereof.

18. A compound having the following formula:



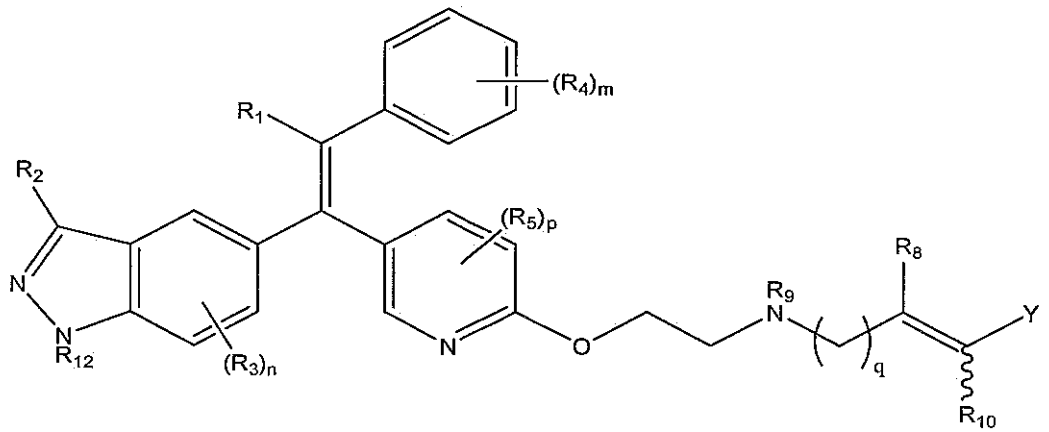
or a pharmaceutically acceptable salt thereof.

19. A compound having the following formula:



or a pharmaceutically acceptable salt thereof.

20. A compound given by formula III:



III

wherein:

R_1 is selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, -CH_2CF_3, and a 4-6 membered heterocyclic ring;

R_2 is selected from the group consisting of H, halogen, hydroxy, C_1-C_3 alkyl, C_3-C_4 cycloalkyl and C_4 heterocyclic ring;

when n is not 0, R_3 are the same or different, and are independently selected from the group consisting of H, halogen, C_1-C_6 alkyl and C_1-C_3 alkoxy optionally substituted with at least one halogen;

n is 0-3;

when m is not zero, R_4 are the same or different and are independently selected from the group consisting of H, halogen, C_1-C_6 alkyl, and OR_{11}, wherein R_{11} is selected from the group consisting of C_3-C_6 cycloalkyl, C_1-C_6 alkyl, aryl, heteroaryl and a 4-6 membered heterocyclic ring;

m is 0-5;

when p is not 0, R_5 are the same or different and are independently selected from the group consisting of H, halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_3-C_4 cycloalkyl, C_3-C_6 cycloalkoxy and C_4 heterocycle;

p is 0-3;

q is 1-2;

R_8 and R_{10} are the same or different and are independently selected from the group consisting of halogen, H and C_1-C_3 alkyl;

R_9 is selected from the group consisting of H, C_1-C_6 alkyl and C_3-C_6 cycloalkyl;

Y is selected from the group consisting of -$S(O)_2R_6$, -$S(O)_2NR_6R_7$, -$C(O)NR_6R_7$,

-$C(O)R_6$, -$C(O)OR_6$, -CN; or wherein Y and R_{10} both represent –CF_3;

R_6 and R_7 are the same or different and are independently selected from the group consisting of H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, aryl, heteroaryl and a 4-6 membered heterocyclic ring wherein said alkyl is saturated or unsaturated or wherein R_6 and R_7 form a 4-6 membered heterocyclic ring with the N to which they are attached, optionally also containing an O atom;

R_{12} is selected from the group consisting of H, C_3-C_4 cycloalkyl and C_1-C_6 alkyl; and

wherein any carbon containing moiety of R_1-R_{12} may be optionally substituted with one or more halogen atoms, fluoromethane, difluoromethane or trifluoromethane, or –OH;

or a pharmaceutically acceptable salt thereof.

21. The compound or pharmaceuticallyl acceptable salt thereof according to claim 20, wherein R_1 is selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, and a 4-6 membered heterocyclic ring.

22. The compound or pharmaceutically acceptable salt thereof according to claim 20 or claim 21, wherein:

R_2 is selected from the group consisting of H, halogen, methyl and ethyl;

R_3 are the same or different, and are independently selected from the group consisting of H, halogen, methyl and ethyl;

R_4 are the same or different and are independently selected from the group consisting of H, halogen, C_1-C_6 alkyl and C_1-C_6 alkoxy;

R_5 are the same or different and are independently selected from the group consisting of H, halogen, methyl and ethyl;

R_8 and R_{10} are the same or different and are independently selected from the group consisting of H and methyl;

R_9 is selected from the group consisting of H, methyl and ethyl; and

R_6 and R_7 are the same or different and are independently selected from the group consisting of H and C_1-C_6 alkyl or wherein R_6 and R_7 form a 4-6 atom heterocyclic ring with the N to which they are attached, optionally also containing an O atom.

23. The compound or pharmaceutically acceptable salt thereof as in one of claims 20-22, wherein Y is $-C(O)NR_6R_7$.

24. The compound or pharmaceutically acceptable salt thereof as in claim 23, wherein R_6 and R_7 are methyl.

25. The compound or pharmaceutically acceptable salt thereof as in any one of claims 23-24, wherein R_8 and R_{10} are both H.

26. The compound or pharmaceutically acceptable salt thereof as in any one of claims 23-25, wherein R_1 is ethyl.

27. The compound or pharmaceutically acceptable salt thereof as in any one of claims 23-25, wherein R_1 is cyclobutyl.

28. The compound or pharmaceutically acceptable salt thereof as in any one of claims 23-27, wherein R_9 is H.

29. The compound or pharmaceutically acceptable salt thereof as in any one of claims 23-28, wherein R_2 is F.

30. The compound or pharmaceutically acceptable salt thereof as in any one of claims 23-28, wherein R_2 is H.

31. The compound or pharmaceutically acceptable salt thereof as in any one of claims 23-30, wherein m is 2, and one of R_4 is F and the other R_4 is Cl.

32. The compound or pharmaceutically acceptable salt thereof as in any one of claims 23-30, wherein m is 2 and both of R_4 are F.

33. The compound or pharmaceutically acceptable salt thereof as in any one of claims 23-30, wherein m is 0.

34. The compound or pharmaceutically acceptable salt thereof as in any one of claims 23-30, wherein n is 1 and R_3 is F.

35. The compound or pharmaceutically acceptable salt thereof as in any one of claims 23-30, wherein n is 0.

36. The compound or pharmaceutically acceptable salt thereof as in any one of claims 23-30, wherein p is 1 and R_5 is F.

37. The compound or pharmaceutically acceptable salt thereof as in any one of claims 23-30, wherein p is 0.

38. A pharmaceutical composition comprising a compound or pharmaceutically acceptable salt according to any one of the preceding claims for use in treating breast cancer.

39. The pharmaceutical composition of claim 38, wherein said breast cancer is an ER-positive breast cancer.

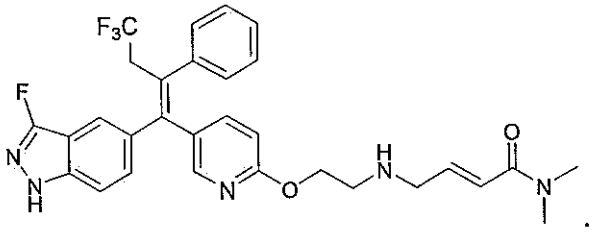
40. The pharmaceutical composition of claim 39, where said ER-positive breast cancer expresses a mutant ER-α protein.

41. Use of a compound or pharmaceutically acceptable salt thereof as in one of claims 1-37 in the manufacture of a medicament for treatment of breast cancer.

42. The use of claim 41, wherein said breast cancer is an ER-positive breast cancer.

43. The use of claim 42, wherein the ER-positive breast cancer expresses a mutant ER-α protein.

44. A compound having the following formula:



45. A pharmaceutical composition comprising a compound or pharmaceutically acceptable salt according to any one of claims 1 to 37 and further comprising a pharmaceutically acceptable excipient.