CLAIMS

1. Use of a gonadotropin-releasing hormone (GnRH) antagonist in the manufacture of a medicament for use in a method of treating an estrogen-dependent disease in a human patient in need thereof, the method comprising:

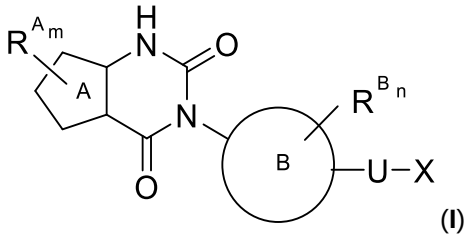
a) periodically administering to the patient a therapeutically effective amount of a gonadotropin-releasing hormone (GnRH) antagonist during a first treatment period,

b) monitoring the patient's bone mineral density at the end of the first treatment period, and, if the patient is determined to exhibit a reduced bone mineral density at the end of the first treatment period relative to a measurement of the patient's bone mineral density obtained during, or prior to commencement of, the first treatment period,

c) periodically administering to the patient a therapeutically effective amount of a GnRH antagonist during a second treatment period, wherein the second treatment period commences at least one week after the end of the first treatment period, and wherein the patient is not administered a GnRH antagonist during the time elapsed between the end of the first treatment period and commencement of the second treatment period.

2. The use of claim 1, wherein the estrogen-dependent disease is uterine fibroids or endometriosis.

3. The use of claim 1 or 2, wherein the GnRH antagonist that is periodically administered to the patient during the first treatment period is not a compound represented by formula (**I**), and the GnRH antagonist that is periodically administered to the patient during the second treatment period is a compound represented by formula (**I**)



(**I**)

wherein ring A is a thiophene ring;

each R^A is independently a halogen atom, a cyano group, a nitro group, an optionally substituted lower alkyl group, an optionally substituted lower alkenyl group, an optionally substituted lower alkynyl group, a hydroxyiminomethyl group, an optionally substituted sulfonyl group, an optionally substituted sulfinyl group, a tetrazolyl group, OW^1, SW^1, COW^1, $COOW^1$, $NHCOW^1$, $NHCONW^2W^3$, NW^2W^3, $CONW^2W^3$, or $SO_2NW^2W^3$, wherein W^1 to W^3 independently are a hydrogen atom or an optionally substituted lower alkyl group, or W^2 and W^3 may bind together with the neighboring nitrogen atom to form an optionally substituted cyclic amino group;

m is an integer from 0 to 3;

ring B is an aryl group or a monocyclic heteroaryl group;

each R^B is independently a halogen atom, a cyano group, an optionally substituted lower alkyl group, OW^4, COW^4, $COOW^4$, or $CONW^5W^6$, wherein W^4 to W^6 independently are a hydrogen atom or an optionally substituted lower alkyl group, or W^5 and W^6 may bind together with the neighboring nitrogen

atom to form an optionally substituted cyclic amino group;

n is an integer from 0 to 2;

U is a single bond;

X is a group represented by —S—L—Y, —O—L—Y, —CO—L—Y, or —SO_2—L—Y, wherein L is an optionally substituted lower alkylene group;

Y is a group represented by Z or —NW^7W^8, wherein W^7 and W^8 independently are a hydrogen atom, an optionally substituted lower alkyl group, or Z with the proviso that W^7 and W^8 are not simultaneously hydrogen atoms, or W^7 and W^8 may bind together with the neighboring nitrogen atom to form an optionally substituted cyclic amino group; and

Z is an optionally fused and optionally substituted cycloalkyl group, an optionally fused and optionally substituted heterocycloalkyl group, an optionally fused and optionally substituted aryl group, or an optionally fused and optionally substituted heteroaryl group;

or a pharmaceutically acceptable salt thereof.

4. Use of a GnRH antagonist in the manufacture of a medicament for use in a method of treating an estrogen-dependent disease in a human patient in need thereof, the method comprising:

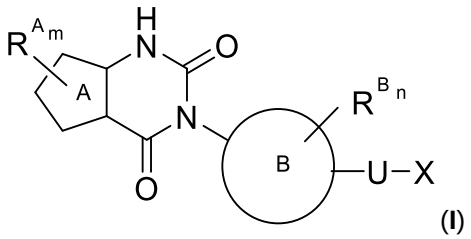
a) periodically administering to the patient a therapeutically effective amount of a GnRH antagonist during a first treatment period,

b) monitoring the patient's bone mineral density at the end of the first treatment period, and, if the patient is determined to exhibit a reduced bone mineral density at the end of the first treatment period relative to a measurement of the patient's bone mineral density obtained during, or prior to commencement of, the first treatment period,

c) periodically administering to the patient a therapeutically effective amount of a GnRH antagonist during a second treatment period, wherein the amount of the GnRH antagonist that is periodically administered to the patient during the second treatment period is less than the amount of the GnRH antagonist that is periodically administered to the patient during the first treatment period.

5. The use of claim 4, wherein the estrogen-dependent disease is uterine fibroids or endometriosis.

6. The use of claim 4 or 5, wherein the GnRH antagonist that is periodically administered to the patient during the first treatment period is not a compound represented by formula (**I**), and the GnRH antagonist that is periodically administered to the patient during the second treatment period is a compound represented by formula (**I**)



(**I**)

wherein ring A is a thiophene ring;

each R^A is independently a halogen atom, a cyano group, a nitro group, an optionally substituted lower alkyl group, an optionally substituted lower alkenyl group, an optionally substituted lower alkynyl group, a hydroxyiminomethyl group, an optionally substituted sulfonyl group, an optionally substituted

sulfinyl group, a tetrazolyl group, OW^1, SW^1, COW^1, $COOW^1$, $NHCOW^1$, $NHCONW^2W^3$, NW^2W^3, $CONW^2W^3$, or $SO_2NW^2W^3$, wherein W^1 to W^3 independently are a hydrogen atom or an optionally substituted lower alkyl group, or W^2 and W^3 may bind together with the neighboring nitrogen atom to form an optionally substituted cyclic amino group;

m is an integer from 0 to 3;

ring B is an aryl group or a monocyclic heteroaryl group;

each R^B is independently a halogen atom, a cyano group, an optionally substituted lower alkyl group, OW^4, COW^4, $COOW^4$, or $CONW^5W^6$, wherein W^4 to W^6 independently are a hydrogen atom or an optionally substituted lower alkyl group, or W^5 and W^6 may bind together with the neighboring nitrogen atom to form an optionally substituted cyclic amino group;

n is an integer from 0 to 2;

U is a single bond;

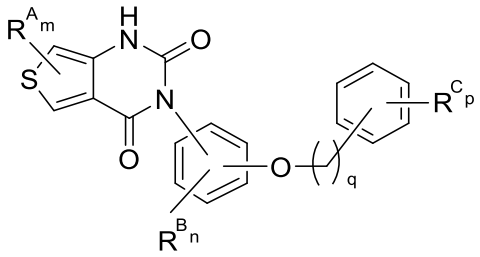
X is a group represented by —S—L—Y, —O—L—Y, —CO—L—Y, or —SO_2—L—Y, wherein L is an optionally substituted lower alkylene group;

Y is a group represented by Z or —NW^7W^8, wherein W^7 and W^8 independently are a hydrogen atom, an optionally substituted lower alkyl group, or Z with the proviso that W^7 and W^8 are not simultaneously hydrogen atoms, or W^7 and W^8 may bind together with the neighboring nitrogen atom to form an optionally substituted cyclic amino group; and

Z is an optionally fused and optionally substituted cycloalkyl group, an optionally fused and optionally substituted heterocycloalkyl group, an optionally fused and optionally substituted aryl group, or an optionally fused and optionally substituted heteroaryl group;

or a pharmaceutically acceptable salt thereof.

7. The use of claim 3 or 4, wherein the compound is represented by formula (**Ia**)



(**Ia**)

wherein each R^A is independently a halogen atom, a cyano group, a nitro group, an optionally substituted lower alkyl group, an optionally substituted lower alkenyl group, an optionally substituted lower alkynyl group, a hydroxyiminomethyl group, an optionally substituted sulfonyl group, an optionally substituted sulfinyl group, a tetrazolyl group, OW^1, SW^1, COW^1, $COOW^1$, $NHCOW^1$, $NHCONW^2W^3$, NW^2W^3, $CONW^2W^3$, or $SO_2NW^2W^3$, wherein W^1 to W^3 independently are a hydrogen atom or an optionally substituted lower alkyl group, or W^2 and W^3 may bind together with the neighboring nitrogen atom to form an optionally substituted cyclic amino group;

m is an integer from 0 to 3;

each R^B is independently a halogen atom, a cyano group, an optionally substituted lower alkyl group, OW^4, COW^4, $COOW^4$, or $CONW^5W^6$, wherein W^4 to W^6 independently are a hydrogen atom or an optionally substituted lower alkyl group, or W^5 and W^6 may bind together with the neighboring nitrogen

atom to form an optionally substituted cyclic amino group;

n is an integer from 0 to 2;

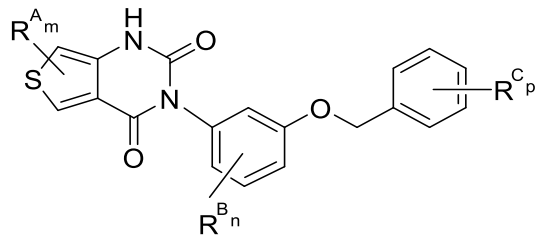
q is an integer from 0 to 3;

each R^C is independently a halogen atom, an optionally substituted lower alkyl group, or OW^9, wherein each W^9 is independently a hydrogen atom or an optionally substituted lower alkyl group; and

p is an integer from 0 to 3;

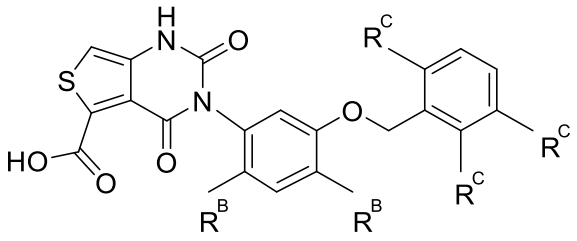
or a pharmaceutically acceptable salt thereof.

8. The use of claim 7, wherein the compound is represented by formula (**Ib**)



(**Ib**).

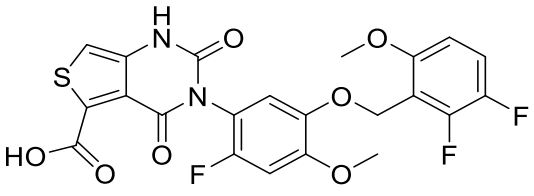
9. The use of claim 8, wherein the compound is represented by formula (**Ic**)



(**Ic**)

or a pharmaceutically acceptable salt thereof.

10. The use of claim 9, wherein the compound is represented by formula (**VI**)



(**VI**)

or a pharmaceutically acceptable salt thereof.

11. The use of claim 10, wherein the compound is the choline salt of the compound represented by formula (**VI**).

12. The use of any one of claims 1 to 11, wherein the compound is administered to the patient once daily during the first treatment period.

13. The use of any one of claims 1 to 12, wherein the compound is administered to the patient in an amount of from about 185 mg to about 215 mg per day during the first treatment period.

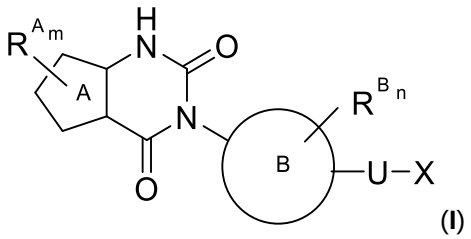
14. The use of any one of claims 1 to 13, wherein the GnRH antagonist is administered to the patient once daily during the second treatment period.

15. The use of any one of claims 1 to 14, wherein the first treatment period has a duration of at least four weeks.

16. The use of any one of claims 1 to 15, wherein the first treatment period has a duration of from about four weeks to about 12 months.

17. A kit comprising a GnRH antagonist and a package insert instructing a user of the kit to administer the GnRH antagonist to a human patient in accordance with the method of any one of claims 1-16.

18. The kit of claim 17, wherein the GnRH antagonist is a compound represented by formula (**I**)



(**I**)

wherein ring A is a thiophene ring;

each R^A is independently a halogen atom, a cyano group, a nitro group, an optionally substituted lower alkyl group, an optionally substituted lower alkenyl group, an optionally substituted lower alkynyl group, a hydroxyiminomethyl group, an optionally substituted sulfonyl group, an optionally substituted sulfinyl group, a tetrazolyl group, OW^1, SW^1, COW^1, $COOW^1$, $NHCOW^1$, $NHCONW^2W^3$, NW^2W^3, $CONW^2W^3$, or $SO_2NW^2W^3$, wherein W^1 to W^3 independently are a hydrogen atom or an optionally substituted lower alkyl group, or W^2 and W^3 may bind together with the neighboring nitrogen atom to form an optionally substituted cyclic amino group;

m is an integer from 0 to 3;

ring B is an aryl group or a monocyclic heteroaryl group;

each R^B is independently a halogen atom, a cyano group, an optionally substituted lower alkyl group, OW^4, COW^4, $COOW^4$, or $CONW^5W^6$, wherein W^4 to W^6 independently are a hydrogen atom or an optionally substituted lower alkyl group, or W^5 and W^6 may bind together with the neighboring nitrogen atom to form an optionally substituted cyclic amino group;

n is an integer from 0 to 2;

U is a single bond;

X is a group represented by —S—L—Y, —O—L—Y, —CO—L—Y, or —SO_2—L—Y, wherein L is an optionally substituted lower alkylene group;

Y is a group represented by Z or —NW^7W^8, wherein W^7 and W^8 independently are a hydrogen atom, an optionally substituted lower alkyl group, or Z with the proviso that W^7 and W^8 are not simultaneously hydrogen atoms, or W^7 and W^8 may bind together with the neighboring nitrogen atom to form an optionally substituted cyclic amino group; and

Z is an optionally fused and optionally substituted cycloalkyl group, an optionally fused and

optionally substituted heterocycloalkyl group, an optionally fused and optionally substituted aryl group, or an optionally fused and optionally substituted heteroaryl group;

or a pharmaceutically acceptable salt thereof.