CLAIMS

1. A method of treating endometriosis in a human patient, wherein the concentration of anti-Müllerian hormone (AMH) in a sample isolated from said patient has been determined, said method comprising:
    a. comparing said concentration of AMH to an AMH reference range; and
    b. administering a higher daily dosage and/or an elevated dosing frequency of a GnRH antagonist to the patient if the concentration of AMH in the sample isolated from the patient is above the AMH reference range; or
    c. administering a lower daily dosage and/or a reduced dosing frequency of a GnRH antagonist to the patient if the concentration of AMH in the sample isolated from the patient is below the AMH reference range.

2. The method of claim 1, said method comprising administering an intermediate quantity and/or an intermediate dosing frequency of a GnRH antagonist to the patient if the concentration of AMH in the sample isolated from the patient is within the AMH reference range.

3. The method of claim 1 or 2, said method comprising administering: from 20 to 700 mg/day of the GnRH antagonist to the patient if the concentration of AMH in the sample isolated from the patient is above the AMH reference range; from 10 to 500 mg/day of the GnRH antagonist to the patient if the concentration of AMH in the sample isolated from said patient is within the AMH reference range; or from 5 to 400 mg/day of a GnRH antagonist to the patient if the concentration of AMH in the sample isolated from said patient is below the AMH reference range.

4. A method of determining a dosing regimen for the treatment of endometriosis in a human patient, wherein the concentration of AMH in a sample isolated from said patient has been determined, said method comprising:
    a. comparing said concentration of AMH to an AMH reference range;
    b. determining that the patient be administered a higher daily dosage and/or an elevated dosing frequency of a GnRH antagonist to the patient if the concentration of AMH in the sample isolated from the patient is above the AMH reference range;
    c. determining that the patient be administered a lower daily dosage and/or a reduced dosing frequency of a GnRH antagonist to the patient if the concentration of AMH in the sample isolated from the patient is below the AMH reference range; or
    d. determining that the patient be administered an intermediate quantity and/or an intermediate dosing frequency of a GnRH antagonist to the patient if the concentration of AMH in the sample isolated from the patient is within the AMH reference range.

5. The method of any one of claims 1-4, wherein said AMH reference range is from 15 to 35 pM.

6. The method of any one of claims 1-5, said method comprising administering said GnRH antagonist to said patient in an amount sufficient to reduce the serum concentration of β17-estradiol (E2) in said patient to between about 20 and about 50 pg/ml, preferably within about 4 to about 36 weeks of said administering.

7. The method of any one of claims 1-6, said method comprising administering said GnRH antagonist to said patient in an amount sufficient to reduce the serum concentration of follicle stimulating hormone (FSH) in said patient to between about 0.1 and about 10 mIU/ml, preferably within about 4 to about 36 weeks of said administering.

8. The method of any one of claims 1-7, said method comprising administering said GnRH antagonist to said patient in an amount sufficient to reduce the serum concentration of luteinizing hormone (LH) in said patient to between about 0.1 and about 10 mIU/ml, preferably within about 4 to about 36 weeks of said administering.

9. The method of any one of claims 1-8, said method comprising administering said GnRH antagonist to said patient in an amount sufficient to reduce endometriosis-associated pain in said patient, preferably within about 4 to about 36 weeks of said administering.

10. The method of claim 9, wherein said endometriosis-associated pain is selected from the group consisting of pelvic pain, dyspareunia, and dyschezia.

11. The method of claim 9 or 10, wherein said endometriosis-associated pain is assessed by determining a Numerical Rating Score (NRS) for said patient.

12. The method of claim 11, wherein said NRS is reduced by from about 1% to about 50%.

13. The method of claim 12, wherein said NRS is reduced by about 30%.

14. The method of claim 9 or 10, wherein said endometriosis-associated pain is assessed by determining a Verbal Rating Score (VRS) for said patient.

15. The method of claim 14, wherein said VRS is reduced by from about 1% to about 50%.

16. The method of claim 15, wherein said VRS is reduced by about 30%.

17. The method of any one of claims 1-16, said method comprising administering said GnRH antagonist to said patient in an amount sufficient to alleviate a symptom selected from the group

consisting of dysmenorrhea, non-menstrual pelvic pain, and dyspareunia, preferably within about 4 to about 36 weeks of said administering.

18. The method of claim 17, wherein said symptom is assessed by determining a Biberoglu and Behrman (B&B) scale score for said patient.

19. The method of claim 18, wherein said B&B scale score is reduced by from about 1% to about 50%.

20. The method of any one of claims 1-19, said method comprising administering said GnRH antagonist to said patient in an amount sufficient to reduce an Endometriosis Health Profile-5 (EHP-5) score determined for said patient, preferably within about 4 to about 36 weeks of said administering.

21. The method of claim 20, wherein said EHP-5 score is reduced by from about 1% to about 50%.

22. The method of any one of claims 1-21, said method comprising administering said GnRH antagonist to said patient in an amount that does not cause a reduction in bone mineral density (BMD) in said patient of greater than 5%.

23. The method of claim 22, said method comprising administering said GnRH antagonist to said patient in an amount that does not cause a reduction in BMD in said patient of greater than 1%.

24. The method of any one of claims 1-23, said method comprising administering add-back therapy to said patient.

25. The method of claim 24, wherein said add-back therapy is administered to said patient concurrently with said GnRH antagonist.

26. The method of claim 24, wherein said add-back therapy is administered to said patient prior to administration of said GnRH antagonist.

27. The method of claim 24, wherein said add-back therapy is administered to said patient following administration of said GnRH antagonist.

28. The method of claim 25, wherein said add-back therapy is administered to said patient in the form of a pharmaceutical composition comprising said GnRH antagonist.

29. The method of any one of claims 24-28, wherein said add-back therapy comprises an estrogen.

30. The method of claim 29, wherein said estrogen is β17-estradiol.

31. The method of any one of claims 24-30, wherein said add-back therapy comprises a progestin.

32. The method of claim 31, wherein said progestin is selected from the group consisting of norethindrone and an ester thereof.

33. The method of claim 32, wherein said progestin is norethindrone acetate.

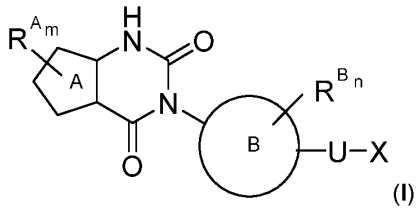
34. The method of any one of claims 24-33, wherein said patient does not exhibit a reduction in BMD of greater than 5% following administration of said GnRH antagonist and said add-back therapy.

35. The method of claim 34, wherein said patient does not exhibit a reduction in BMD of greater than 1% following administration of said GnRH antagonist and said add-back therapy.

36. The method of any one of claims 22, 23, 34, and 35, wherein said BMD is assessed by dual energy X-ray absorptiometry.

37. The method of any one of claims 22, 23, and 34-36, wherein said BMD is assessed in the spine or femur of said patient.

38. The method of any one of claims 1-37, wherein said 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;

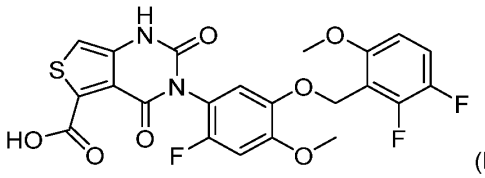
X is a group represented by —S—L—Y, —O—L—Y, —CO—L—Y, or —SO_2—L—Y, wherein L is an optionally substituted lower alkylene group;

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;

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.

39. The method of claim 38, wherein said compound is represented by formula (**II**)



(**II**)

or a pharmaceutically acceptable salt thereof.

40. The method of claim 39, wherein said compound is the choline salt of the compound represented by formula (**II**).

41. The method of any one of claims 38-40, said method comprising administering from 85 to 115 mg/day or from 185 to 215 mg/day of said GnRH antagonist to said patient if the concentration of AMH in the sample isolated from said patient is above the AMH reference range.

42. The method of claim 41, said method comprising administering 100 mg/day or 200 mg/day of said GnRH antagonist to said patient if the concentration of AMH in the sample isolated from said patient is above the AMH reference range.

43. The method of any one of claims 38-42, said method comprising administering from 35 to 65 mg/day of said GnRH antagonist to said patient if the concentration of AMH in the sample isolated from said patient is below the AMH reference range.

44. The method of claim 43, said method comprising administering 50 mg/day of said GnRH antagonist to said patient if the concentration of AMH in the sample isolated from said patient is below the AMH reference range.

45. The method of any one of claims 38-44, said method comprising administering from 60 to 90 mg/day or from 85 to 115 mg/day of said GnRH antagonist to said patient if the concentration of AMH in the sample isolated from said patient is within the AMH reference range.

46. The method of claim 45, said method comprising administering 75 mg/day or 100 mg/day of said GnRH antagonist to said patient if the concentration of AMH in the sample isolated from said patient is within the AMH reference range.

47. The method of any one of claims 1-37, wherein said GnRH antagonist is selected from the group consisting of elagolix, relugolix, ASP-1707, SKI2670, and BAY-784, or a derivative or variant thereof.

48. The method of claim 47, wherein said GnRH antagonist is elagolix.

49. The method of claim 48, said method comprising administering 150 mg/day or more of said GnRH antagonist to said patient if the concentration of AMH in the sample isolated from said patient is above the AMH reference range.

50. The method of claim 48, said method comprising administering 400 mg/day or more of said GnRH antagonist to said patient if the concentration of AMH in the sample isolated from said patient is above the AMH reference range.

51. The method of any one of claims 48-50, said method comprising administering 150 mg/day or less of said GnRH antagonist to said patient if the concentration of AMH in the sample isolated from said patient is below the AMH reference range.

52. The method of any one of claims 48-50, said method comprising administering 400 mg/day or less of said GnRH antagonist to said patient if the concentration of AMH in the sample isolated from said patient is below the AMH reference range.

53. The method of any one of claims 48-52, said method comprising administering 150 mg/day of said GnRH antagonist to said patient if the concentration of AMH in the sample isolated from said patient is within the AMH reference range.

54. The method of any one of claims 48-52, said method comprising administering 400 mg/day of said GnRH antagonist to said patient if the concentration of AMH in the sample isolated from said patient is within the AMH reference range.

55. The method of claim 47, wherein said GnRH antagonist is relugolix.

56. The method of claim 55, said method comprising administering 40 mg/day or more of said GnRH antagonist to said patient if the concentration of AMH in the sample isolated from said patient is above the AMH reference range.

57. The method of claim 55 or 56, said method comprising administering 40 mg/day or less of said GnRH antagonist to said patient if the concentration of AMH in the sample isolated from said patient is below the AMH reference range.

58. The method of any one of claims 55-57, said method comprising administering 40 mg/day of said GnRH antagonist to said patient if the concentration of AMH in the sample isolated from said patient is within the AMH reference range.

59. The method of claim 47, wherein said GnRH antagonist is ASP-1707.

60. The method of claim 59, said method comprising administering 10 mg/day or more of said GnRH antagonist to said patient if the concentration of AMH in the sample isolated from said patient is above the AMH reference range.

61. The method of claim 59 or 60, said method comprising administering 10 mg/day or less of said GnRH antagonist to said patient if the concentration of AMH in the sample isolated from said patient is below the AMH reference range.

62. The method of any one of claims 59-61, said method comprising administering 10 mg/day of said GnRH antagonist to said patient if the concentration of AMH in the sample isolated from said patient is within the AMH reference range.

63. The method of any one of claims 1-62, said method comprising orally administering said GnRH antagonist to said patient.

64. The method of any one of claims 1-62, said method comprising intravenously administering said GnRH antagonist to said patient.

65. A kit comprising one or more agents capable of detecting AMH and a package insert, wherein said package insert instructs a user of said kit to perform the method of any one of claims 1-64.

66. The kit of claim 65, wherein said kit further comprises one or more agents capable of detecting a compound selected from the group consisting of E2, LH, and FSH.

67. The kit of claim 65 or 66, wherein said kit further comprises said GnRH antagonist.

68. A method of treating endometriosis in a human patient undergoing therapy with a GnRH antagonist, wherein the concentration of E2 in a sample isolated from said patient has been determined, said method comprising:

a. comparing said concentration of E2 to an E2 reference range; and
b. administering an increased dose of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is above the E2 reference range, or administering a decreased dose of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is below the E2 reference range.

69. The method of claim 68, said method comprising administering the originally dispensed dose of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is within the E2 reference range.

70. The method of claim 69, wherein said originally dispensed dose of said GnRH antagonist is from 10 to 500 mg/day.

71. The method of claim 70, wherein said originally dispensed dose of said GnRH antagonist is 75 mg/day.

72. A method of optimizing a dosing regimen for the treatment of endometriosis in a human patient undergoing therapy with a GnRH antagonist, wherein the concentration of E2 in a sample isolated from said patient has been determined, said method comprising:

a. comparing said concentration of E2 to an E2 reference range;
b. determining that the patient be administered an increased dose of a GnRH antagonist if the concentration of E2 in the sample isolated from said patient is above the E2 reference range, determining that the patient be administered a decreased dose of a GnRH antagonist if the concentration of E2 in the sample isolated from said patient is below the E2 reference range, or determining that the patient be administered the originally dispensed dose of said GnRH antagonist if the concentration of E2 in the sample isolated from said patient is within the E2 reference range; and optionally
c. administering said GnRH antagonist to said patient at the dose determined in (b).

73. The method of any one of claims 68-72, wherein said sample was isolated from the patient between about 4 and about 36 weeks following the start of said GnRH antagonist therapy.

74. The method of claim 73, wherein said sample was isolated from the patient about 4 weeks following the start of said GnRH antagonist therapy.

75. The method of claim 73, wherein said sample was isolated from the patient about 8 weeks following the start of said GnRH antagonist therapy.

76. The method of claim 73, wherein said sample was isolated from the patient about 12 weeks following the start of said GnRH antagonist therapy.

77. The method of claim 73, wherein said sample was isolated from the patient about 24 weeks following the start of said GnRH antagonist therapy.

78. The method of any one of claims 68-77, wherein said administering is performed between about 4 weeks and about 36 weeks following the start of said GnRH antagonist therapy.

79. The method of claim 78, wherein said administering is performed about 12 weeks following the start of said GnRH antagonist therapy.

80. The method of claim 78, wherein said administering is performed about 24 weeks following the start of said GnRH antagonist therapy.

81. The method of any one of claims 68-80, wherein said E2 reference range is from 20 to 50 pg/ml.

82. The method of any one of claims 68-81, said method comprising administering said GnRH antagonist to said patient in an amount sufficient to reduce the serum concentration of E2 in said patient to between about 20 and about 50 pg/ml, preferably within about 4 to about 36 weeks of said administering.

83. The method of any one of claims 68-82, said method comprising administering said GnRH antagonist to said patient in an amount sufficient to reduce the serum concentration of FSH in said patient to between about 0.1 and about 10 mIU/ml, preferably within about 4 to about 36 weeks of said administering.

84. The method of any one of claims 68-83, said method comprising administering said GnRH antagonist to said patient in an amount sufficient to reduce the serum concentration of LH in said patient to between about 0.1 and about 10 mIU/ml, preferably within about 4 to about 36 weeks of said administering.

85. The method of any one of claims 68-84, said method comprising administering said GnRH antagonist to said patient in an amount sufficient to reduce endometriosis-associated pain in said patient, preferably within about 4 to about 36 weeks of said administering.

86. The method of claim 85, wherein said endometriosis-associated pain is selected from the group consisting of pelvic pain, dyspareunia, and dyschezia.

87. The method of claim 85 or 86, wherein said endometriosis-associated pain is assessed by determining a Numerical Rating Score (NRS) for said patient.

88. The method of claim 87, wherein said NRS is reduced by from about 1% to about 50%.

89. The method of claim 88, wherein said NRS is reduced by about 30%.

90. The method of claim 85 or 86 wherein said endometriosis-associated pain is assessed by determining a Verbal Rating Score (VRS) for said patient.

91. The method of claim 90, wherein said VRS is reduced by from about 1% to about 50%.

92. The method of claim 91, wherein said VRS is reduced by about 30%.

93. The method of any one of claims 68-92, said method comprising administering said GnRH antagonist to said patient in an amount sufficient to alleviate a symptom selected from the group consisting of dysmenorrhea, non-menstrual pelvic pain, and dyspareunia, preferably within about 4 to about 36 weeks of said administering.

94. The method of claim 93, wherein said symptom is assessed by determining a Biberoglu and Behrman (B&B) scale score for said patient.

95. The method of claim 94, wherein said B&B scale score is reduced by from about 1% to about 50%.

96. The method of any one of claims 68-95, said method comprising administering said GnRH antagonist to said patient in an amount sufficient to reduce an Endometriosis Health Profile-5 (EHP-5) score determined for said patient, preferably within about 4 to about 36 weeks of said administering.

97. The method of claim 96, wherein said EHP-5 score is reduced by from about 1% to about 50%.

98. The method of any one of claims 68-97, said method comprising administering said GnRH antagonist to said patient in an amount that does not cause a reduction in BMD in said patient of greater than 5%.

99. The method of claim 98, said method comprising administering said GnRH antagonist to said patient in an amount that does not cause a reduction in BMD in said patient of greater than 1%.

100. The method of any one of claims 68-99, said method comprising administering add-back therapy to said patient.

101. The method of claim 100, wherein said add-back therapy is administered to said patient concurrently with said GnRH antagonist.

102. The method of claim 100, wherein said add-back therapy is administered to said patient prior to administration of said GnRH antagonist.

103. The method of claim 100, wherein said add-back therapy is administered to said patient following administration of said GnRH antagonist.

104. The method of claim 101, wherein said add-back therapy is administered to said patient in the form of a pharmaceutical composition comprising said GnRH antagonist.

105. The method of any one of claims 68-104, wherein said add-back therapy comprises an estrogen.

106. The method of claim 105, wherein said estrogen is β17-estradiol.

107. The method of any one of claims 100-106, wherein said add-back therapy comprises a progestin.

108. The method of claim 107, wherein said progestin is selected from the group consisting of norethindrone and an ester thereof.

109. The method of claim 108, wherein said progestin is norethindrone acetate.

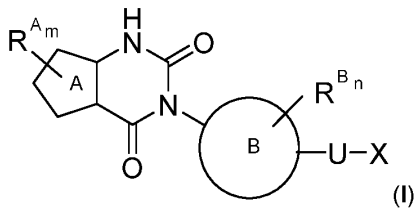
110. The method of any one of claims 100-109, wherein said patient does not exhibit a reduction in BMD of greater than 5% following administration of said GnRH antagonist and said add-back therapy.

111. The method of claim 110, wherein said patient does not exhibit a reduction in BMD of greater than 1% following administration of said GnRH antagonist and said add-back therapy.

112. The method of claim any one of claims 98, 99, 110, and 111, wherein said BMD is assessed by dual energy X-ray absorptiometry.

113. The method of any one of claims 98, 99, and 110-112, wherein said BMD is assessed in the spine or femur of said patient.

114. The method of any one of claims 68-113, wherein said 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;

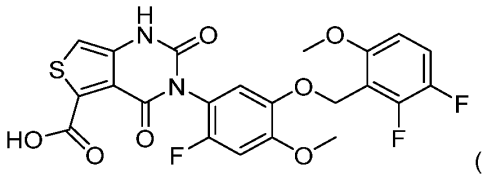
X is a group represented by —S—L—Y, —O—L—Y, —CO—L—Y, or —SO_2—L—Y, wherein L is an optionally substituted lower alkylene group;

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;

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.

115. The method of claim 114, wherein said compound is represented by formula (**II**)



(II)

or a pharmaceutically acceptable salt thereof.

116. The method of claim 115, wherein said compound is the choline salt of the compound represented by formula (II).

117. The method of any one of claims 114-116, said method comprising administering from 85 to 115 mg/day or from 185 to 215 mg/day of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is above the E2 reference range.

118. The method of claim 117, said method comprising administering 100 mg/day or 200 mg/day of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is above the E2 reference range.

119. The method of any one of claims 114-118, said method comprising administering from 35 to 65 mg/day of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is below the E2 reference range.

120. The method of claim 119, said method comprising administering 50 mg/day of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is below the E2 reference range.

121. The method of any one of claims 114-120, said method comprising administering from 60 to 90 mg/day or from 85 to 115 mg/day of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is within the E2 reference range.

122. The method of claim 121, said method comprising administering 75 mg/day or 100 mg/day of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is within the E2 reference range.

123. The method of any one of claims 68-113, wherein said GnRH antagonist is selected from the group consisting of elagolix, relugolix, ASP-1707, SKI2670, and BAY-784.

124. The method of claim 123, wherein said GnRH antagonist is elagolix.

125. The method of claim 124, said method comprising administering 150 mg/day or more of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is above the E2 reference range.

126. The method of claim 124, said method comprising administering 400 mg/day or more of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is above the E2 reference range.

127. The method of any one of claims 124-126, said method comprising administering 150 mg/day or less of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is below the E2 reference range.

128. The method of any one of claims 124-126, said method comprising administering 400 mg/day or less of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is below the E2 reference range.

129. The method of any one of claims 124-128, said method comprising administering 150 mg/day of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is within the E2 reference range.

130. The method of any one of claims 124-128, said method comprising administering 400 mg/day of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is within the E2 reference range.

131. The method of claim 123, wherein said GnRH antagonist is relugolix.

132. The method of claim 131, said method comprising administering 40 mg/day or more of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is above the E2 reference range.

133. The method of claim 131 or 132, said method comprising administering 40 mg/day or less of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is below the E2 reference range.

134. The method of any one of claims 131-133, said method comprising administering 40 mg/day of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is within the E2 reference range.

135. The method of claim 123, wherein said GnRH antagonist is ASP-1707.

136. The method of claim 135, said method comprising administering 10 mg/day or more of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is above the E2 reference range.

137. The method of claim 135 or 136, said method comprising administering 10 mg/day or less of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is below the E2 reference range.

138. The method of any one of claims 135-137, said method comprising administering 10 mg/day of said GnRH antagonist to said patient if the concentration of E2 in the sample isolated from said patient is within the E2 reference range.

139. The method of any one of claims 68-138, said method comprising orally administering said GnRH antagonist to said patient.

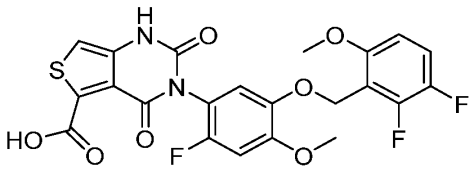
140. The method of any one of claims 68-138, said method comprising intravenously administering said GnRH antagonist to said patient.

141. A kit comprising one or more agents capable of detecting E2 and a package insert, wherein said package insert instructs a user of said kit to perform the method of any one of claims 68-140.

142. The kit of claim 141, wherein said kit further comprises one or more agents capable of detecting a compound selected from the group consisting of LH and FSH.

143. The kit of claim 141 or 142, wherein said kit further comprises said GnRH antagonist.

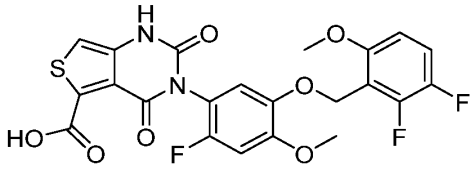
144. A method of treating endometriosis in a human patient, said method comprising administering to said patient a compound represented by formula (**II**),



(**II**)

or a pharmaceutically acceptable salt thereof, optionally wherein the compound is choline 3-[2-fluoro-5-(2,3-difluoro-6-methoxybenzyloxy)4-methoxyphenyl]-2,4-dioxo-1,2,3,4- tetrahydrothieno [3,4d]pyrimidine-5-carboxylate, in an amount of from about 50 mg/day to about 200 mg/day.

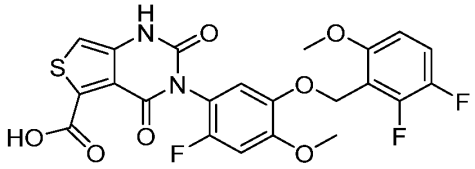
145. A method of reducing the concentration of E2, follicle-stimulating hormone (FSH), and/or luteinizing hormone (LH) in the blood of a human patient, said method comprising administering to said patient a compound represented by formula (**II**),



(**II**)

or a pharmaceutically acceptable salt thereof, optionally wherein the compound is choline 3-[2-fluoro-5-(2,3-difluoro-6-methoxybenzyloxy)4-methoxyphenyl]-2,4-dioxo-1,2,3,4- tetrahydrothieno [3,4d]pyrimidine-5-carboxylate, in an amount of from about 50 mg/day to about 200 mg/day.

146. A method of reducing endometriosis-associated pain in a human patient in need thereof, said method comprising administering to said patient a compound represented by formula (**II**),



(**II**)

or a pharmaceutically acceptable salt thereof, optionally wherein the compound is choline 3-[2-fluoro-5-(2,3-difluoro-6-methoxybenzyloxy)4-methoxyphenyl]-2,4-dioxo-1,2,3,4- tetrahydrothieno [3,4d]pyrimidine-5-carboxylate, in an amount of from about 50 mg/day to about 200 mg/day.

147. The method of any one of claims 144-146, wherein said compound is administered to said patient in an amount of about 50 mg/day.

148. The method of any one of claims 144-146, wherein said compound is administered to said patient in an amount of about 75 mg/day.

149. The method of any one of claims 144-146, wherein said compound is administered to said patient in an amount of about 100 mg/day.

150. The method of any one of claims 144-146, wherein said compound is administered to said patient in an amount of about 200 mg/day.

151. The method of any one of claims 144-150, wherein said compound is choline 3-[2-fluoro-5-(2,3-difluoro-6-methoxybenzyloxy)4-methoxyphenyl]-2,4-dioxo-1,2,3,4- tetrahydrothieno [3,4d]pyrimidine-5-carboxylate and is in a crystalline state.

152. The method of claim 151, wherein said compound exhibits characteristic X-ray powder diffraction peaks at about 7.1° 2θ, about 11.5° 2θ, about 19.4° 2θ, about 21.5° 2θ, about 22.0° 2θ, about 22.6° 2θ, about 23.5° 2θ, and about 26.2° 2θ.

153. The method of claim 151 or 152, wherein said compound exhibits ^{13}C solid-state NMR peaks centered at about 55.5 ppm, about 57.1 ppm, about 58.7 ppm, about 69.8 ppm, about 98.1 ppm, about 110.3 ppm, about 111.6 ppm, about 113.7 ppm, about 118.0 ppm, about 145.3 ppm, about 149.8 ppm, and about 155.8 ppm.

154. The method of any one of claims 151-153, wherein said compound salt exhibits ^{19}F solid-state NMR peaks centered at about -151.8 ppm, -145.2 ppm, and -131.6 ppm.

155. The method of any one of claims 144-154, wherein said compound is orally administered to said patient.

156. The method of any one of claims 144-155, said method comprising administering add-back therapy to said patient.

157. The method of claim 156, wherein said add-back therapy is administered to said patient one or more times daily.

158. The method of claim 157, wherein said add-back therapy is administered to said patient once daily, concurrently with said compound.

159. The method of claim 157, wherein said add-back therapy is administered to said patient once daily, prior to administration of said compound.

160. The method of claim 157, wherein said add-back therapy is administered to said patient once daily, following administration of said compound.

161. The method of claim 158, wherein said add-back therapy is administered to said patient in the form of a pharmaceutical composition comprising said compound.

162. The method of any one of claims 156-161, wherein said add-back therapy comprises an estrogen.

163. The method of claim 162, wherein said estrogen is selected from the group consisting of β17-estradiol, ethinyl estradiol, and conjugated estrogens.

164. The method of claim 163, wherein said estrogen is β17-estradiol.

165. The method of claim 164, wherein said β17-estradiol is administered to said patient at a dose of about 1.0 mg/day.

166. The method of claim 164, wherein said β17-estradiol is administered to said patient at a dose of about 0.5 mg/day.

167. The method of claim 163, wherein said estrogen is ethinyl estradiol.

168. The method of claim 167, wherein said ethinyl estradiol is administered to said patient at a dose of about 5.0 µg/day.

169. The method of claim 167, wherein said ethinyl estradiol is administered to said patient at a dose of about 2.5 µg/day.

170. The method of claim 163, wherein said estrogen is a conjugated estrogen.

171. The method of claim 170, wherein said conjugated estrogen is administered to said patient at a dose of about 0.625 mg/day.

172. The method of claim 170, wherein said conjugated estrogen is administered to said patient at a dose of about 0.45 mg/day.

173. The method of claim 170, wherein said conjugated estrogen is administered to said patient at a dose of about 0.3 mg/day

174. The method of any one of claims 156-173, wherein said add-back therapy comprises a progestin.

175. The method of claim 174, wherein said progestin is selected from the group consisting of norethindrone or an ester thereof, progesterone, norgestimate, medroxyprogesterone, and drospirenone.

176. The method of claim 175, wherein said progestin is norethindrone or norethindrone acetate.

177. The method of claim 176, wherein said norethindrone or norethindrone acetate is administered to said patient at a dose of about 1.0 mg/day.

178. The method of claim 176, wherein said norethindrone or norethindrone acetate is administered to said patient at a dose of about 0.5 mg/day.

179. The method of claim 176, wherein said norethindrone or norethindrone acetate is administered to said patient at a dose of about 0.1 mg/day.

180. The method of claim 175, wherein said progestin is progesterone.

181. The method of claim 180, wherein said progesterone is administered to said patient at a dose of about 200 mg/day.

182. The method of claim 180, wherein said progesterone is administered to said patient at a dose of about 100 mg/day.

183. The method of claim 175, wherein said progestin is norgestimate.

184. The method of claim 183, wherein said norgestimate is administered to said patient at a dose of about 0.09 mg/day.

185. The method of claim 175, wherein said progestin is medroxyprogesterone.

186. The method of claim 185, wherein said medroxyprogesterone is administered to said patient at a dose of about 5 mg/day.

187. The method of claim 185, wherein said medroxyprogesterone is administered to said patient at a dose of about 2.5 mg/day.

188. The method of claim 185, wherein said medroxyprogesterone is administered to said patient at a dose of about 1.5 mg/day.

189. The method of claim 175, wherein said progestin is drospirenone.

190. The method of claim 189, wherein said drospirenone is administered to said patient at a dose of about 0.5 mg/day.

191. The method of claim 189, wherein said drospirenone is administered to said patient at a dose of about 0.25 mg/day.

192. The method of any one of claims 156-161, wherein said add-back therapy comprises about 1.0 mg of β17-estradiol and about 0.5 mg of norethindrone acetate.

193. The method of any one of claims 156-161, wherein said add-back therapy comprises about 0.5 mg of β17-estradiol and about 0.1 mg of norethindrone acetate.

194. The method of any one of claims 144-193, wherein said patient exhibits reduced pelvic pain following administration of said compound to said patient.

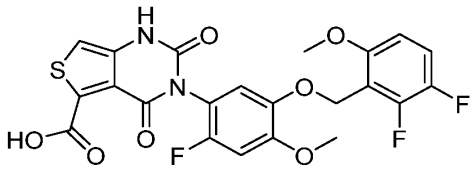
195. The method of any one of claims 144-194, wherein said patient exhibits reduced back pain following administration of said compound to said patient.

196. The method of any one of claims 144-195, wherein said patient does not exhibit a reduction in BMD of greater than 5% following administration of said compound to said patient.

197. The method of claim 196, wherein said patient does not exhibit a reduction in BMD of greater than 1% following administration of said compound to said patient.

198. The method of claim 196 or 197, wherein said BMD is assessed by dual energy X-ray absorptiometry.

199. A kit comprising a compound represented by formula (**II**),



(**II**)

or a pharmaceutically acceptable salt thereof, optionally wherein the compound is choline 3-[2-fluoro-5-(2,3-difluoro-6-methoxybenzyloxy)4-methoxyphenyl]-2,4-dioxo-1,2,3,4- tetrahydrothieno [3,4d]pyrimidine-5-carboxylate, and a package insert instructing a user of said kit to perform the method of any one of claims 144-198.

200. The kit of claim 199, wherein the compound is choline 3-[2-fluoro-5-(2,3-difluoro-6-methoxybenzyloxy)4-methoxyphenyl]-2,4-dioxo-1,2,3,4- tetrahydrothieno [3,4d]pyrimidine-5-carboxylate.