CLAIMS

1. The compound 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile for use in the treatment of hypogonadism in a male patient with serum total testosterone levels below 400 ng/dl, wherein the compound is provided in a form comprising from about 0.0005 mg to about 2.0 mg 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile per dose, and wherein the compound is for administration according to a dosing regimen having a dosing periodicity ranging from about one dose once daily to about one dose once every 60 days.

2. The compound for use according to claim 1, wherein the treatment is for an overweight or obese male patient.

3. The compound for use according to claim 1 or 2, wherein the treatment is for hypogonadotropic hypogonadism.

4. The compound for use according to any one of claims 1 to 3, wherein the male patient has a serum total testosterone level below 300 ng/dl.

5. The compound for use according to any of claims 1 to 4, wherein the administration of the compound increases the serum total testosterone level by at least 10% in comparison to the serum total testosterone level prior to administration of the compound, preferably wherein the serum total testosterone level is normalized.

6. The compound for use according to any one of the preceding claims, wherein the compound is for the prevention or treatment of one or more disorders selected from metabolic syndrome, type II diabetes, obesity and cardiovascular disease.

7. The compound for use according to any one of the preceding claims, wherein the compound is for (i) the prevention or treatment of one or more disorders selected from insulin resistance, glucose intolerance and dyslipidaemia, and/or (ii) the improvement of insulin sensitivity and/or glucose metabolism and/or the lipid profile.

8. The compound for use according to any one of the preceding claims, wherein the compound is for the prevention or treatment of one or more disorders selected from the group consisting of decreased libido, decreased spontaneous erections, erectile dysfunction, decreased fertility, loss of body hair, reduced shaving, lack of energy, fatigue, impaired cognition, depression, changes in mood, low bone mineral density, increased risk of fractures, decreased muscle mass, decreased muscle strength, increased abdominal fat mass and limited body performance capacity.

9. The compound for use according to any one of the preceding claims, wherein the patient is a male human.

10. The compound for use according to any one of the preceding claims, wherein the compound is provided in a form comprising from about 0.001 mg to about 1.0 mg, more preferably from about 0.005 mg to about 0.5 mg, most preferably from about 0.01 mg to about 0.1 mg, or from about 0.005 mg to less than 0.05 mg 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile per dose.

11. The compound for use according to any one of the preceding claims, wherein the compound is for administration according to a dosing regimen having a dosing periodicity selected from a dosing periodicity of about one dose once daily, about one dose once every 2 days, about one dose once every 5 days, about one dose once weekly, about one dose once biweekly, about one dose once every 3 weeks, about one dose once every 4 weeks, about one dose once monthly and about one dose once every 6 weeks, preferably about one dose once weekly or once biweekly.

12. An oral pharmaceutical composition comprising from about 0.0005 mg to about 2.0 mg, preferably from about 0.001 mg to about 1.0 mg, more preferably from about 0.005 mg to about 0.5 mg, most preferably from about 0.01 mg to about 0.1 mg, or from about 0.005 mg to less than 0.05 mg 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile per dose, optionally in combination with one or more pharmaceutically acceptable excipients, for use in the treatment of hypogonadism in a male patient having serum total testosterone levels below 400 ng/dl, and wherein the composition is for administration according to a dosing regimen having a dosing periodicity from about one dose once daily to about one dose once every 60 days.

13. A kit of parts for use in the treatment of hypogonadism in a male patient having serum total testosterone levels below 400 ng/dl, comprising:

(i) a pharmaceutical composition comprising 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)-methylene]-bisbenzonitrile wherein the composition is for administration according to a dosing regimen having a dosing periodicity from about one dose once daily to about one dose once every 60 days; together with

(ii) instructions how to administer said pharmaceutical composition.

14. Use of the compound 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile for the manufacture of a medicament for the treatment of hypogonadism in a male patient with serum total testosterone levels below 400 ng/dl, wherein the compound is provided in a form comprising from about 0.0005 mg to about 2.0 mg 4,4'-[fluoro-

(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile per dose, and wherein the compound is for administration according to a dosing regimen having a dosing periodicity ranging from about one dose once daily to about one dose once every 60 days.

15. The use according to claim 16, wherein the treatment is for an overweight or obese male patient.

16. The use according to claim 14 or 15, wherein the treatment is for hypogonadotropic hypogonadism.

17. The use according to any one of claims 14 to 16, wherein the male patient has a serum total testosterone level below 300 ng/dl.

18. The use according to any one of claims 14 to 17, wherein the administration of the compound increases the serum total testosterone level by at least 10% in comparison to the serum total testosterone level prior to administration of the compound, preferably wherein the serum total testosterone level is normalized.

19. The use according to any one of the preceding claims 14 to 18, wherein the compound is for the prevention or treatment of one or more disorders selected from metabolic syndrome, type II diabetes, obesity and cardiovascular disease.

20. The use according to any one of the preceding claims 14 to 19, wherein the compound is for (i) the prevention or treatment of one or more disorders selected from insulin resistance, glucose intolerance and dyslipidaemia, and/or (ii) the improvement of insulin sensitivity and/or glucose metabolism and/or the lipid profile.

21. The use according to any one of the preceding claims 14 to 20, wherein the compound is for the prevention or treatment of one or more disorders selected from the group consisting of decreased libido, decreased spontaneous erections, erectile dysfunction, decreased fertility, loss of body hair, reduced shaving, lack of energy, fatigue, impaired cognition, depression, changes in mood, low bone mineral density, increased risk of fractures, decreased muscle mass, decreased muscle strength, increased abdominal fat mass and limited body performance capacity.

22. The use according to any one of the preceding claims 14 to 21, wherein the patient is a male human.

23. The use according to any one of the preceding claims 14 to 22, wherein the compound is provided in a form comprising from about 0.001 mg to about 1.0 mg, more preferably from about 0.005 mg to about 0.5 mg, most preferably from about

0.01 mg to about 0.1 mg, or from about 0.005 mg to less than 0.05 mg 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile per dose.

24. The use according to any one of the preceding claims 14 to 23, wherein the compound is for administration according to a dosing regimen having a dosing periodicity selected from a dosing periodicity of about one dose once daily, about one dose once every 2 days, about one dose once every 5 days, about one dose once weekly, about one dose once biweekly, about one dose once every 3 weeks, about one dose once every 4 weeks, about one dose once monthly and about one dose once every 6 weeks, preferably about one dose once weekly or one dose once biweekly.

25. A method for the treatment of hypogonadism in a male patient with serum total testosterone levels below 400 ng/dl and in need of increased testosterone levels comprising administering to said patient an effective amount of the compound 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile, wherein the effective amount of the compound is from about 0.0005mg to about 2.0 mg per dose, and wherein the compound is administered according to a dosing regimen having a dosing periodicity selected from about one dose once daily to about one dose once every 60 days.

26. The method of claim 25, wherein the male patient is overweight or obese.

27. The method of claim 25, wherein the method is for the treatment of hypogonadotropic hypogonadism.

28. The method of claim 25, wherein the method is for the treatment of hypogonadotropic hypogonadism in an overweight or obese male patient.

29. The method of claim 25, wherein the testosterone level is increased by at least 10% in comparison to the testosterone level prior to administration of the compound.

30. The method of claim 25, wherein the testosterone level is normalized.

31. The method of claim 25, wherein the patient is in need of the prevention or treatment of one or more disorders selected from metabolic syndrome, type II diabetes, obesity and cardiovascular disease.

32. The method of claim 25, wherein the patient is in need of the prevention or treatment of one more disorders selected from insulin resistance, glucose intolerance and dyslipidaemia.

33. The method of claim 25, wherein the patient is in need of improved insulin sensitivity.

34. The method of claim 25, wherein the patient is in need of improved glucose metabolism.

35. The method of claim 25, wherein the patient is in need of an improved lipid profile.

36. The method of claim 25, wherein the patient is in need of the prevention or treatment of one or more disorders selected from the group consisting of decreased libido, decreased spontaneous erections, erectile dysfunction, decreased fertility, loss of body hair, reduced shaving, lack of energy, fatigue, impaired cognition, depression, changes in mood, low bone mineral density, increased risk of fractures, decreased muscle mass, decreased muscle strength, increased abdominal fat mass and limited body performance capacity.

37. The method of claim 25, wherein the patient is in need of increased muscle mass and strength.

38. The method of claim 25, wherein the patient is in need of a normalized body composition.

39. The method of claim 25, wherein the patient is in need of a decrease in abdominal fat mass.

40. The method of claim 25, wherein the patient is in need of an improved sexual function and desire.

41. The method of claim 25, wherein the patient is in need of increased fertility.

42. The method of claim 25, wherein the patient is in need of increased bone mineral density.

43. The method of claim 25, wherein the patient is a male human.

44. The method of claim 25, wherein the effective amount of 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile is from about 0.001 mg to about 1.0 mg per dose.

45. The method of claim 25, wherein the effective amount of 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile is from 0.005 mg to about 0.5 mg per dose.

46. The method of claim 25, wherein the effective amount of 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile is from about 0.01 mg to about 0.1 mg per dose.

47. The method of claim 25, wherein the effective amount of 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile is from about 0.005 mg to less than 0.05 mg per dose.

48. The method of claim 25, wherein the effective amount of 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile is orally administered to the patient.

49. The method of claim 25, wherein 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile is administered according to a dosing regimen having a dosing periodicity ranging from about one dose once every 2 days to about one dose once every 40 days.

50. The method of claim 25, wherein 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile is administered according to a dosing regimen having a dosing periodicity selected from about one dose once every 5 days, about one dose once weekly, about one dose once every 10 days, about one dose once biweekly, about one dose once every 3 weeks, about one dose once every 4 weeks, about one dose once monthly and about one dose once every 6 weeks.

51. The method of claim 25, wherein 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile is administered according to a dosing regimen having a dosing periodicity of about one dose once weekly.

52. The method of claim 25, wherein 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile is administered according to a dosing regimen having a dosing periodicity of about one dose once biweekly.

53. The method of claim 25, wherein 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile is administered according to a dosing regimen having a dosing periodicity of about one dose once monthly.

54. The method of claim 25, wherein 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile, when administered to the patient, shows an apparent elimination half-life of at least about 14 days.

55. The method of claim 25, wherein 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile when administered to the patient shows an apparent elimination half-life of at least about 20 days.

56. The method of claim 25, wherein 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile when administered to the patient shows an apparent elimination half-life of at least about 25 days.

57. The method of claim 25, wherein 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile when administered to the patient shows an apparent elimination half-life of at least about 30 days.

58. The method of claim 25, wherein when administering a single dose of 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile, said dose results in an increased effective blood concentration of testosterone over a period of time from 3 to 30 days.

59. The method of claim 58, wherein the serum concentration of testosterone is increased by at least 10% over the serum testosterone concentration prior to administration of the compound.

60. The method of claim 25, wherein an effective amount of 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile from about 0.001 mg to about 1.0 mg per dose is administered according to a dosing regimen having a dosing periodicity ranging from about one dose once every 2 days to about one dose once every 40 days.

61. The method of claim 25, wherein an effective amount of 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile from about 0.005 mg to about 0.5 mg per dose is administered according to a dosing regimen having a dosing periodicity selected from about one dose once every 5 days, about one dose once weekly, about one dose once every 10 days, about one dose once biweekly, about one dose once every 3 weeks, about one dose once every 4 weeks, about one dose once monthly and about one dose once every 6 weeks.

62. The method of claim 25, wherein an effective amount of 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile from about 0.01 mg to about 0.1 mg per dose is administered according to a dosing regimen having a dosing periodicity ranging from about one dose once weekly to about one dose once monthly.

63. The method of claim 25, wherein an effective amount of 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile from about 0.005 mg to less than 0.05 mg per dose is administered according to a dosing regimen having a dosing periodicity ranging from about one dose once weekly to about one dose once monthly.

64. The method of claim 25, wherein an effective amount of 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile of less than 0.05 mg per dose is administered according to a dosing regimen having a dosing periodicity of about one dose once weekly.

65. The method of claim 25, wherein an effective amount of 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile of less than 0.05 mg per dose is administered according to a dosing regimen having a dosing periodicity of about one dose once biweekly.

66. The method of claim 25, wherein 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile is administered in combination with another active ingredient.

67. The method of claim 25, wherein an effective amount of 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile is administered for a treatment period of at least about two months, preferably from at least about three months to about twelve months.

68. The method of claim 25, wherein an effective amount of 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile is administered continuously.

CLAIMS

1. The use of 4,4'-[fluoro(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile in the manufacture of a medicament for the treatment of hypogonadism in a male patient with serum total testosterone levels below 400 ng/dl, wherein the compound is provided in a form comprising from about 0.0005 mg to about 2.0 mg 4,4'-[fluoro(1-H-1,2,4-triazol-1-yl)methylene]bis-benzonitrile per dose, and wherein the compound is to be administered according to a dosing regimen having a dosing periodicity ranging from about one dose once daily to about one dose once every 60 days.

2. The use according to claim 1, wherein the treatment is for an over-weight or obese male patient.

3. The use according to claim 1 or claim 2, wherein the treatment is for hypogonadotropic hypogonadism.

4. The use according to any one of the preceding claims, wherein the male patient has a serum total testosterone level below 300 ng/dl.

5. The use according to any of the preceding claims, wherein the administration of the compound increases the serum total testosterone level by at least 10% in comparison to the serum total testosterone level prior to administration of the compound, preferably wherein the serum total testosterone level is normalized.

6. The use according to any one of the preceding claims, wherein the compound is for the prevention or treatment of one or more disorders selected from metabolic syndrome, type II diabetes, obesity and cardiovascular disease.

7. The use according to any one of the preceding claims, wherein the compound is for (i) the prevention or treatment of one or more disorders selected from insulin resistance, glucose intolerance and dyslipidaemia, and/or (ii) the improvement of insulin sensitivity and/or glucose metabolism and/or the lipid profile.

8. The use according to any one of the preceding claims, wherein the compound is for the prevention or treatment of one or more disorders selected from the group consisting of decreased libido, decreased spontaneous erections, erectile

dysfunction, decreased fertility, loss of body hair, reduced shaving, lack of energy, fatigue, impaired cognition, depression, changes in mood, low bone mineral density, increased risk of fractures, decreased muscle mass, decreased muscle strength, increased abdominal fat mass and limited body performance capacity.

9. The use according to any one of the preceding claims, wherein the patient is a male human.

10. The compound for use according to any one of the preceding claims, wherein the compound is provided in a form comprising from about 0.001 mg to about 1.0 mg, more preferably from about 0.005 mg to about 0.5 mg, most preferably from about 0.01 mg to about 0.1 mg, or from about 0.005 mg to less than 0.05 mg 4,4'-[fluoro-(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile per dose.

11. The use according to any one of the preceding claims, wherein the compound is to be administered according to a dosing regimen having a dosing periodicity selected from a dosing periodicity of about one dose once daily, about one dose once every 2 days, about one dose once every 5 days, about one dose once weekly, about one dose once biweekly, about one dose once every 3 weeks, about one dose once every 4 weeks, about one dose once monthly and about one dose once every 6 weeks, preferably about one dose once weekly or once biweekly.

12. An oral pharmaceutical composition comprising from about 0.0005 mg to about 2.0 mg, preferably from about 0.001 mg to about 1.0 mg, more preferably from about 0.005 mg to about 0.5 mg, most preferably from about 0.01 mg to about 0.1 mg, or from about 0.005 mg to less than 0.05 mg 4,4'-[fluoro(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile per dose, optionally in combination with one or more pharmaceutically acceptable excipients, for use in the treatment of hypogonadism in a male patient having serum total testosterone levels below 400 ng/dl, and wherein the composition is to be administered according to a dosing regimen having a dosing periodicity from about one dose once daily to about one dose once every 60 days.

13. The use of a kit of parts comprising:
(i) a pharmaceutical composition comprising 4,4'-[fluoro(1-H-1,2,4-triazol-1-yl)-methylene]-bisbenzonitrile wherein the composition is for administration according to

a dosing regimen having a dosing periodicity from about one dose once daily to about one dose once every 60 days; together with
(ii) instructions how to administer said pharmaceutical composition;
in the manufacture of a medicament for use in the treatment of hypogonadism in a male patient having serum total testosterone levels below 400 ng/dl.

14. The use according to claim 1, wherein the effective amount of 4,4'-[fluoro(1-H-1,2,4-tria-zol-1-yl)methylene]bisbenzonitrile is to be orally administered to the patient.

15. The use according to claim 1, wherein 4,4'-[fluoro(1-H-1,2,4-triazol-1-yl)methyl-ene]bis-benzonitrile is to be administered according to a dosing regimen having a dosing periodicity ranging from about one dose once every 2 days to about one dose once every 40 days.

16. The use according to claim 1, wherein 4,4'-[fluoro(1-H-1,2,4-triazol-1-yl)methyl-ene]bis-benzonitrile, when administered to the patient, shows an apparent elimination half-life of at least about 14 days.

17. The use according to claim 1, wherein 4,4'-[fluoro(1-H-1,2,4-triazol-1-yl)methyl-ene]bis-benzonitrile when administered to the patient shows an apparent elimination half-life of at least about 20 days.

18. The use according to claim 1, wherein 4,4'-[fluoro(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile when administered to the patient shows an apparent elimination half-life of at least about 25 days.

19. The use according to claim 1, wherein 4,4'-[fluoro(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile when administered to the patient shows an apparent elimination half-life of at least about 30 days.

20. The use according to claim 1, wherein when administering a single dose of 4,4'-[fluoro(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile, said dose results in an increased effective blood concentration of testosterone over a period of time from 3 to 30 days.

21. The use according to claim 1, wherein an effective amount of 4,4'-[fluoro(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile from about 0.001 mg to about 1.0 mg per dose is to be administered according to a dosing regimen having a dosing periodicity ranging from about one dose once every 2 days to about one dose once every 40 days.

22. The use according to claim 1, wherein 4,4'-[fluoro(1-H-1,2,4-triazol-1-yl)methylene]bisbenzonitrile is to be administered in combination with another active ingredient.

23. The use according to claim 1, wherein an effective amount of 4,4'-[fluoro(1-H-1,2,4-tria-zol-1-yl)methylene]bisbenzonitrile is to be administered for a treatment period of at least about two months, preferably from at least about three months to about twelve months.

24. The use according to claim 1, wherein an effective amount of 4,4'-[fluoro(1-H-1,2,4-tria-zol-1-yl)methylene]bisbenzonitrile is to be administered continuously.