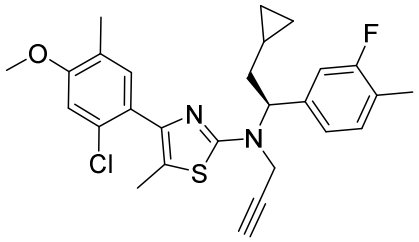
CLAIMS

1. A compound that is 4-(2-chloro-4-methoxy-5-methylphenyl)-*N*-[(1*S*)-2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl]-5-methyl-*N*-prop-2-ynyl-1,3-thiazol-2-amine (**Compound 1**):



Compound 1 ;

or a pharmaceutically acceptable salt thereof, wherein the enantiomeric excess (e.e.%) of the compound is at least 99.4% as determined by chiral HPLC.

2. The compound according to claim 1, wherein **Compound 1**, or a pharmaceutically acceptable salt thereof, is the free base.

3. The compound according to claim 1 or 2, wherein the enantiomeric excess (e.e.%) of **Compound 1**, or a pharmaceutically acceptable salt thereof, is at least 99.5%.

4. The compound according to claim 1 or 2, wherein the enantiomeric excess (e.e.%) of **Compound 1**, or a pharmaceutically acceptable salt thereof, is at least 99.6%.

5. The compound according to claim 1 or 2, wherein the enantiomeric excess (e.e.%) of **Compound 1**, or a pharmaceutically acceptable salt thereof, is at least 99.7%.

6. The compound according to claim 1 or 2, wherein the enantiomeric excess (e.e.%) of **Compound 1**, or a pharmaceutically acceptable salt thereof, is at least 99.8%.

7. The compound according to claim 1 or 2, wherein the enantiomeric excess (e.e.%) of **Compound 1**, or a pharmaceutically acceptable salt thereof, is at least 99.9%.

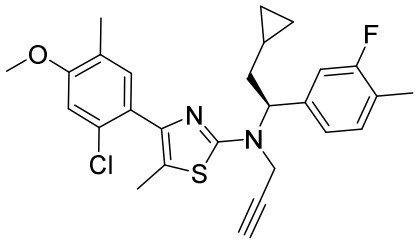
8. The compound according to claim 1 or 2, wherein the enantiomeric excess (e.e.%) of **Compound 1**, or a pharmaceutically acceptable salt thereof, is 99.9%.

9. The compound according to any one of claims 1 to 8, wherein the enantiomeric excess (e.e.%) of **Compound 1**, or a pharmaceutically acceptable salt thereof, is 100%.

10. The compound according to any one of claims 1 to 9, wherein **Compound 1**, or a pharmaceutically acceptable salt thereof, is crystalline.

11. The compound according to any one of claims 1 to 10, wherein **Compound 1**, or a pharmaceutically acceptable salt thereof, is crystalline Form I.

12. A composition comprising a compound that is 4-(2-chloro-4-methoxy-5-methylphenyl)-*N*-[(1*S*)-2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl]-5-methyl-*N*-prop-2-ynyl-1,3-thiazol-2-amine (**Compound 1**) according to any one of claims 1 to 11:

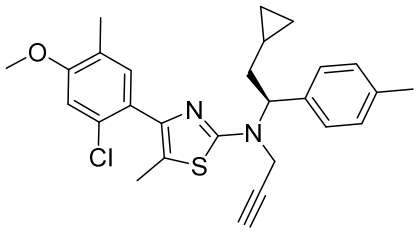


Compound 1 ;

or a pharmaceutically acceptable salt thereof.

13. The composition according to claim 12, wherein **Compound 1**, or a pharmaceutically acceptable salt thereof, is the free base.

14. The composition according to claim 12 or 13, further comprising a compound that is (*S*)-4-(2-chloro-4-methoxy-5-methylphenyl)-*N*-(2-cyclopropyl-1-(*p*-tolyl)ethyl)-5-methyl-*N*-(prop-2-yn-1-yl)thiazol-2-amine (**Compound IIa**), or a pharmaceutically acceptable salt thereof:



Compound IIa .

15. The composition according to claim 14, wherein **Compound IIa**, or a pharmaceutically acceptable salt thereof, is present in the composition in an amount ranging from 1.0% to 0.4%.

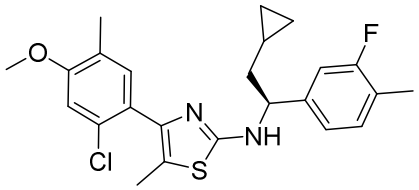
16. The composition according to claim 14, wherein **Compound IIa**, or a pharmaceutically acceptable salt thereof, is present in the composition in an amount ranging from 0.9% to 0.4%.

17. The composition according to claim 14, wherein **Compound IIa**, or a pharmaceutically acceptable salt thereof, is present in the composition in an amount ranging from 0.8% to 0.4%.

18. The composition according to claim 14, wherein **Compound IIa**, or a pharmaceutically acceptable salt thereof, is present in the composition in an amount ranging from 0.7% to 0.4%.

19. The composition according to claim 14, wherein **Compound IIa**, or a pharmaceutically acceptable salt thereof, is present in the composition in an amount ranging from 0.6% to 0.4%.

20. The composition according to any one of claims 12 to 19, further comprising a compound that is (*S*)-4-(2-chloro-4-methoxy-5-methylphenyl)-*N*-(2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl)-5-methylthiazol-2-amine (**Compound 9A**), or a pharmaceutically acceptable salt thereof:



9A

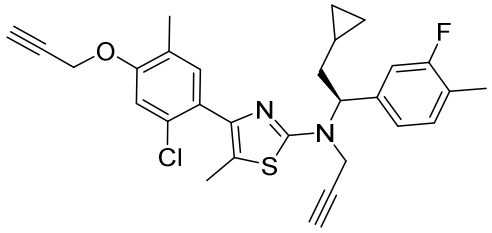
21. The composition according to claim 20, wherein **Compound 9A**, or a pharmaceutically acceptable salt thereof, is present in the composition in an amount less than 0.5%.

22. The composition according to claim 20, wherein **Compound 9A**, or a pharmaceutically acceptable salt thereof, is present in the composition in an amount less than 0.3%.

23. The composition according to claim 20, wherein **Compound 9A**, or a pharmaceutically acceptable salt thereof, is present in the composition in an amount less than 0.1%.

24. The composition according to claim 20, wherein **Compound 9A**, or a pharmaceutically acceptable salt thereof, is present in the composition in an amount less than 0.05%.

25. The composition according to any one of claims 12 to 24, further comprising a compound that is (*S*)-4-(2-chloro-5-methyl-4-(prop-2-yn-1-yloxy)phenyl)-*N*-(2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl)-5-methyl-*N*-(prop-2-yn-1-yl)thiazol-2-amine (**Compound IIb**), or a pharmaceutically acceptable salt thereof:



Compound IIb ;

wherein the compound is present in the composition in an amount less than 0.1%.

26. The composition according to claim 25, wherein **Compound IIb**, or a pharmaceutically acceptable salt thereof, is present in the composition in an amount less than 0.05%.

27. The composition according to any one of claims 12 to 26, further comprising ethanol.

28. The composition according to claim 27, wherein ethanol is present in the composition in an amount ranging from 300 ppm to 5000 ppm.

29. The composition according to claim 27, wherein ethanol is present in the composition in an amount ranging from 300 ppm to 3000 ppm.

30. The composition according to claim 27, wherein ethanol is present in the composition in an amount ranging from 300 ppm to 2000 ppm.

31. The composition according to claim 27, wherein ethanol is present in the composition in an amount ranging from 300 ppm to 1000 ppm.

32. The composition according to claim 27, wherein ethanol is present in the composition in an amount ranging from 350 ppm to 600 ppm.

33. The composition according to claim 27, wherein ethanol is present in the composition in an amount ranging from 375 ppm to 550 ppm.

34. The composition according to any one of claims 12 to 33, further comprising propargyl bromide, wherein propargyl bromide is present in the composition in an amount less than 10 ppm.

35. A composition according to claim 12, further comprising at least one compound selected from:

(*S*)-4-(2-chloro-4-methoxy-5-methylphenyl)-*N*-(2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl)-5-methylthiazol-2-amine (**Compound 9A**), or a pharmaceutically acceptable salt thereof;

(*S*)-4-(2-chloro-4-methoxy-5-methylphenyl)-*N*-(2-cyclopropyl-1-(*p*-tolyl)ethyl)-5-methyl-*N*-(prop-2-yn-1-yl)thiazol-2-amine (**Compound IIa**), or a pharmaceutically acceptable salt thereof;

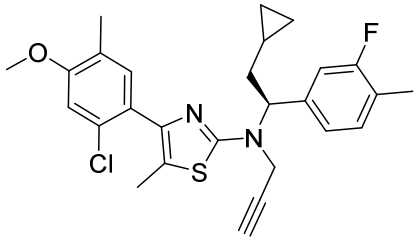
(*S*)-4-(2-chloro-5-methyl-4-(prop-2-yn-1-yloxy)phenyl)-*N*-(2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl)-5-methyl-*N*-(prop-2-yn-1-yl)thiazol-2-amine (**Compound IIb**), or a pharmaceutically acceptable salt thereof;

ethanol; and

propargyl bromide.

36. The composition according to claim 35, wherein **Compound 1**, or a pharmaceutically acceptable salt thereof, is the free base.

37. A compound that is 4-(2-chloro-4-methoxy-5-methylphenyl)-*N*-[(1*S*)-2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl]-5-methyl-*N*-prop-2-ynyl-1,3-thiazol-2-amine (**Compound 1**) according to any one of claims 1 to 11:

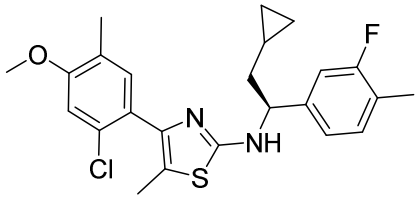


Compound 1 ;

or a pharmaceutically acceptable salt thereof,

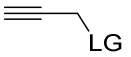
prepared by a process comprising:

alkylating (*S*)-4-(2-chloro-4-methoxy-5-methylphenyl)-*N*-(2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl)-5-methylthiazol-2-amine (**Compound 9A**) or a salt thereof:



9A ,

with a Compound of Formula (**Ii**):



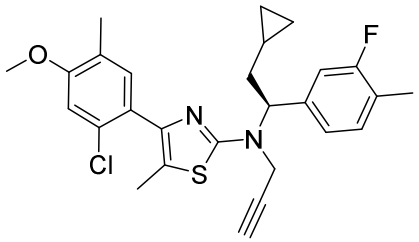
(Ii) ,

wherein: LG is a leaving group;

in the presence of an alkylating-step solvent, a phase-transfer catalyst, an alkylating-step base, and water to form 4-(2-chloro-4-methoxy-5-methylphenyl)-*N*-[(1*S*)-2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl]-5-methyl-*N*-prop-2-ynyl-1,3-thiazol-2-amine (**Compound 1**) or a pharmaceutically acceptable salt thereof.

38. The compound according to claim 37, wherein **Compound 1**, or a pharmaceutically acceptable salt thereof, is the free base.

39. A composition comprising the compound that is 4-(2-chloro-4-methoxy-5-methylphenyl)-*N*-[(1*S*)-2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl]-5-methyl-*N*-prop-2-ynyl-1,3-thiazol-2-amine (**Compound 1**) according to any one of claims 1 to 11:

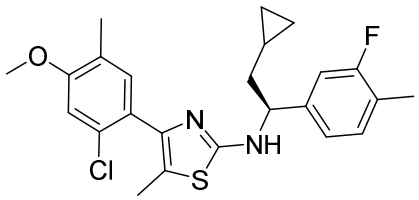


Compound 1 ;

or a pharmaceutically acceptable salt thereof,

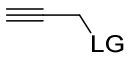
prepared by a process comprising:

alkylating (*S*)-4-(2-chloro-4-methoxy-5-methylphenyl)-*N*-(2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl)-5-methylthiazol-2-amine (**Compound 9A**) or a salt thereof:



9A ,

with a Compound of Formula (**Ii**):



(Ii) ,

wherein: LG is a leaving group;

in the presence of an alkylating-step solvent, a phase-transfer catalyst, an alkylating-step base, and water to form 4-(2-chloro-4-methoxy-5-methylphenyl)-*N*-[(1*S*)-2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl]-5-methyl-*N*-prop-2-ynyl-1,3-thiazol-2-amine (**Compound 1**) or a pharmaceutically acceptable salt thereof.

40. The composition according to claim 39, wherein **Compound 1**, or a pharmaceutically acceptable salt thereof, is the free base.

41. A pharmaceutical product selected from:

a pharmaceutical composition, a formulation, a unit dosage form, and a kit;

each comprising **Compound 1**, according to any one of claims 1 to 11, 37, and 38, or a pharmaceutically acceptable salt thereof.

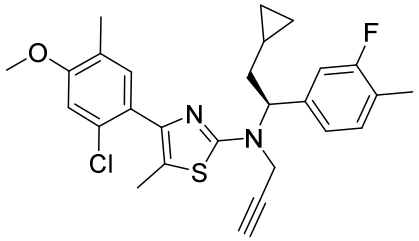
42. The pharmaceutical product according to claim 41, wherein **Compound 1**, or a pharmaceutically acceptable salt thereof, is the free base.

43. The pharmaceutical product according to claim 41 or 42, wherein the pharmaceutical product is adapted for oral administration.

44. A pharmaceutical composition comprising **Compound 1**, according to any one of claims 1 to 11, 37, and 38 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

45. A pharmaceutical composition comprising:

(a) a compound that is 4-(2-chloro-4-methoxy-5-methylphenyl)-*N*-[(1*S*)-2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl]-5-methyl-*N*-prop-2-ynyl-1,3-thiazol-2-amine (**Compound 1**) according to any one of claims 1 to 11:



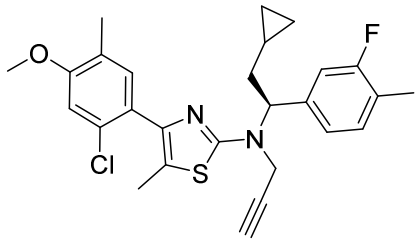
Compound 1,

or a pharmaceutically acceptable salt thereof; and

(b) one or more of an oily phase vehicle, an emulsifying agent, a nonionic surfactant, and a solubilizing agent.

46. A pharmaceutical composition in oral solution dosage form comprising:

(a) a compound that is 4-(2-chloro-4-methoxy-5-methylphenyl)-*N*-[(1*S*)-2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl]-5-methyl-*N*-prop-2-ynyl-1,3-thiazol-2-amine (**Compound 1**) according to any one of claims 1 to 11:



Compound 1

,

or a pharmaceutically acceptable salt thereof;

(b) one or more of a sweetener, an anti-oxidant, and a flavor; and

(c) a liquid vehicle, wherein the liquid vehicle is selected from medium-chain triglycerides, propylene glycol dicaprylate/dicaprate, glycerin, propylene glycol, polyethylene glycol, olive oil, soybean oil, corn oil, and transcutol.

47. The pharmaceutical composition according to any one of claims 44 to 46, wherein **Compound 1**, or a pharmaceutically acceptable salt thereof, is the free base.

48. A compound according to any one of claims 1 to 11, 37, and 38, or a pharmaceutically acceptable salt thereof;
a composition according to any one of claims 12 to 36, 39, and 40;
a pharmaceutical product according to any one of claims 41 to 43; or
a pharmaceutical composition according to any one of claims 44 to 47;
for use in a method of treatment or prophylaxis of the human or animal body by therapy.

49. A compound according to any one of claims 1 to 11, 37, and 38, or a pharmaceutically acceptable salt thereof;
a composition according to any one of claims 12 to 36, 39, and 40;
a pharmaceutical product according to any one of claims 41 to 43; or
a pharmaceutical composition according to any one of claims 44 to 47;
for use in a method of treatment of a disorder in a subject wherein the subject has abnormal levels of CRF_1.

50. A compound according to any one of claims 1 to 11, 37, and 38, or a pharmaceutically acceptable salt thereof;
a composition according to any one of claims 12 to 36, 39, and 40;
a pharmaceutical product according to any one of claims 41 to 43; or
a pharmaceutical composition according to any one of claims 44 to 47;
for use in a method of treatment of a Corticotropin Releasing Factor 1 (CRF_1) disorder.

51. A compound according to any one of claims 1 to 11, 37, and 38, or a pharmaceutically acceptable salt thereof;
a composition according to any one of claims 12 to 36, 39, and 40;
a pharmaceutical product according to any one of claims 41 to 43; or
a pharmaceutical composition according to any one of claims 44 to 47;
for use in a method of treating congenital adrenal hyperplasia (CAH).

52. The compound, or a pharmaceutically acceptable salt thereof; the composition; the pharmaceutical product; or the pharmaceutical composition for use according to claim 51;

wherein the congenital adrenal hyperplasia is classic congenital adrenal hyperplasia.

53. The compound, or a pharmaceutically acceptable salt thereof; the composition; the pharmaceutical product; or the pharmaceutical composition for use according to claim 51 or 52;

wherein the method of treating congenital adrenal hyperplasia comprises administering a glucocorticoid.

54. The use of a compound according to any one of claims 1 to 11, 37, and 38, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of a subject wherein the subject has abnormal levels of CRF_1.

55. The use of a compound according to any one of claims 1 to 11, 37, and 38 or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of a Corticotropin Releasing Factor 1 (CRF_1) disorder.

56. The use of a compound according to any one of claims 1 to 11, 37, and 38 or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of congenital adrenal hyperplasia (CAH).

57. The use according to claim 56, wherein the congenital adrenal hyperplasia is classic congenital adrenal hyperplasia.

58. The use according to claim 56 or 57, wherein the treatment of congenital adrenal hyperplasia comprises administering a glucocorticoid.

59. A method of treating a disorder in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of:
a compound according to any one of claims 1 to 11, 37, and 38, or a pharmaceutically acceptable salt thereof;
a composition according to any one of claims 12 to 36, 39, and 40;
a pharmaceutical product according to any one of claims 41 to 43; or
a pharmaceutical composition according to any one of claims 44 to 47;
wherein the subject has abnormal levels of CRF_1.

60. A method of treating a Corticotropin Releasing Factor 1 (CRF_1) disorder in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of:
a compound according to any one of claims 1 to 11, 37, and 38, or a pharmaceutically acceptable salt thereof;
a composition according to any one of claims 12 to 36, 39, and 40;
a pharmaceutical product according to any one of claims 41 to 43; or
a pharmaceutical composition according to any one of claims 44 to 47.

61. A method of treating congenital adrenal hyperplasia (CAH), in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of:
a compound according to any one of claims 1 to 11, 37, and 38, or a pharmaceutically acceptable salt thereof;
a composition according to any one of claims 12 to 36, 39, and 40;
a pharmaceutical product according to any one of claims 41 to 43; or
a pharmaceutical composition according to any one of claims 44 to 47.

62. The method according to claim 61, wherein the congenital adrenal hyperplasia is classic congenital adrenal hyperplasia.

63. The method according to claim 61 or 62, wherein the method further comprises administering to the subject a glucocorticoid.

64. A method for preparing a pharmaceutical composition comprising the step of admixing a compound according to any one of claims 1 to 11, 37, and 38, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.