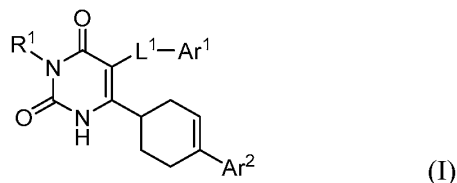


WHAT IS CLAIMED IS:

1 1. A compound of formula I:



3 or a pharmaceutically acceptable salt thereof, or an isomer thereof,

4 wherein

5 R¹ is H or C₁₋₆ alkyl;

6 L¹ is C₁₋₄ alkylene;

7 Ar¹ is a C₆₋₁₂ aryl or 5-10 membered heteroaryl having 1-4 heteroatoms selected from

8 N, O, and S, each of which is optionally substituted with 1-3 R^a groups;

9 each R^a is independently H, halogen, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkyl, C₁₋₄

10 haloalkoxy, -SO₂R^{a1}, or -NR^{a1}R^{a2};

11 R^{a1} and R^{a2} are each independently H or C₁₋₄ alkyl; or R^{a1} and R^{a2} when attached to a

12 nitrogen atom are combined to form a 3-6 membered heterocycle having 1-2

13 heteroatoms selected from N, O, and S, which is optionally substituted with 1-

14 2 R^{a3};

15 each R^{a3} is independently H, halogen, C₁₋₄ alkyl, or C₁₋₄ alkoxy;

16 Ar² is a C₆₋₁₂ aryl or 5-10 membered heteroaryl having 1-4 heteroatoms selected from

17 N, O, and S, each of which is optionally substituted with 1-4 R^b groups;

18 each R^b is independently H, halogen, CN, hydroxy, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄

19 alkynyl, C₁₋₄ alkoxy, C₁₋₄ alkoxy-C₁₋₄ alkyl, C₁₋₄ hydroxyalkyl, C₁₋₄ haloalkyl,

20 C₁₋₄ haloalkoxy, -OR^{b4}, -NR^{b1}R^{b2}, -C(O)R^{b1}, -C(O)OR^{b1}, -OC(O)R^{b1}, -

21 C(O)NR^{b1}R^{b2}, -NR^{b1}C(O)R^{b2}, -SO₂R^{b1}, -SO₂NR^{b1}R^{b2}, or C₃₋₆ cycloalkyl;

22 alternatively, two R^b groups on adjacent ring atoms can be combined to form a C₅₋₈

23 cycloalkyl or a 5-8 membered heterocycle having 1-2 heteroatoms selected

24 from N, O, and S;

25 R^{b1} and R^{b2} are each independently H or C₁₋₄ alkyl; or R^{b1} and R^{b2} when attached to a

26 nitrogen atom are combined to form a 3-6 membered heterocycle having 1-2

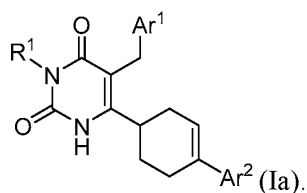
27 heteroatoms selected from N, O, and S, which is optionally substituted with 1-

28 2 R^{b3};

29 each R^{b3} is independently H, halogen, C₁₋₄ alkyl, or C₁₋₄ alkoxy; and
 30 each R^{b4} is independently C₁₋₄ hydroxyalkyl, C₁₋₄ alkoxy-C₁₋₄ alkyl, C₃₋₆ cycloalkyl or
 31 C₃₋₆ cycloalkyl-C₁₋₄ alkyl.

1 2. The compound of claim 1, or a pharmaceutically acceptable salt
 2 thereof, or an isomer thereof, wherein
 3 R¹ is H or C₁₋₆ alkyl;
 4 L¹ is C₁₋₄ alkylene;
 5 Ar¹ is a C₆₋₁₂ aryl or 5-10 membered heteroaryl having 1-4 heteroatoms selected from
 6 N, O, and S, each of which is optionally substituted with 1-3 R^a groups;
 7 each R^a is independently H, halogen, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkyl, C₁₋₄
 8 haloalkoxy, -SO₂R^{a1}, or -NR^{a1}R^{a2};
 9 R^{a1} and R^{a2} are each independently H or C₁₋₄ alkyl; or R^{a1} and R^{a2} when attached to a
 10 nitrogen atom are combined to form a 3-6 membered heterocycle having 1-2
 11 heteroatoms selected from N, O, and S, which is optionally substituted with 1-
 12 2 R^{a3};
 13 each R^{a3} is independently H, halogen, C₁₋₄ alkyl, or C₁₋₄ alkoxy;
 14 Ar² is a C₆₋₁₂ aryl or 5-10 membered heteroaryl having 1-4 heteroatoms selected from
 15 N, O, and S, each of which is optionally substituted with 1-4 R^b groups;
 16 each R^b is independently H, halogen, CN, hydroxy, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄
 17 alkynyl, C₁₋₄ alkoxy, -C₁₋₄ hydroxyalkyl, C₁₋₄ haloalkyl, C₁₋₄ haloalkoxy, -
 18 NR^{b1}R^{b2}, -C(O)R^{b1}, -C(O)OR^{b1}, -OC(O)R^{b1}, -C(O)NR^{b1}R^{b2}, -NR^{b1}C(O)R^{b2}, -
 19 SO₂R^{b1}, or -SO₂NR^{b1}R^{b2};
 20 R^{b1} and R^{b2} are each independently H or C₁₋₄ alkyl; or R^{b1} and R^{b2} when attached to a
 21 nitrogen atom are combined to form a 3-6 membered heterocycle having 1-2
 22 heteroatoms selected from N, O, and S, which is optionally substituted with 1-
 23 2 R^{b3};
 24 each R^{b3} is independently H, halogen, C₁₋₄ alkyl, or C₁₋₄ alkoxy.

1 3. The compound of claim 1 or 2, having formula Ia:



1 4. The compound of any one of claims 1 to 3, wherein Ar¹ is phenyl or 5-
2 6 membered heteroaryl having 1-4 heteroatoms selected from N, O, and S, each of which is
3 optionally substituted with 1-3 R^a groups.

1 5. The compound of any one of claims 1 to 4, wherein Ar¹ is phenyl or 5-
2 6 membered heteroaryl having 1-2 heteroatoms selected from N and S, each of which is
3 optionally substituted with 1-2 R^a groups.

1 6. The compound of any one of claims 1 to 5, wherein Ar¹ is phenyl,
2 pyridinyl, or thiazolyl, each of which is optionally substituted with 1-2 R^a groups.

1 7. The compound of any one of claims 1 to 6, wherein Ar¹ is phenyl,
2 which is optionally substituted with 1-2 R^a groups.

1 8. The compound of any one of claims 1 to 7, wherein
2 each R^a is independently H, halogen, CN, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkyl,
3 or -NR^{a1}R^{a2}; and
4 R^{a1} and R^{a2} are each independently H or C₁₋₄ alkyl.

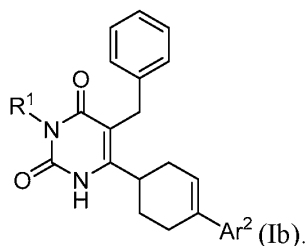
1 9. The compound of any one of claims 1 to 8, wherein each R^a is
2 independently H, F, Cl, CN, Me, Et, OMe, CF₃, NH₂, or N(Me)₂.

1 10. The compound of any one of claims 1 to 7, wherein
2 each R^a is independently H, halogen, C₁₋₄ haloalkyl, or -NR^{a1}R^{a2}; and
3 R^{a1} and R^{a2} are combined to form a 3-6 membered heterocycle having 1-2
4 heteroatoms selected from N and O.

1 11. The compound of any one of claims 1 to 7 and 10, wherein each R^a is
2 independently H, F, CF₃, or 1-pyrrolidinyl.

1 12. The compound of any one of claims 1 to 11, wherein Ar¹ is phenyl.

13. The compound of any one of claims 1 to 12, having formula Ib:



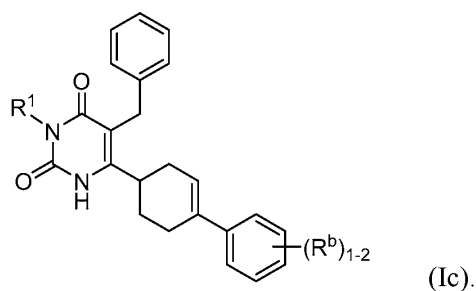
14. The compound of any one of claims 1 to 13, wherein Ar² is a phenyl or 5-9 membered heteroaryl having 1-4 heteroatoms selected from N, O, and S, each of which is optionally substituted with 1-4 R^b groups.

15. The compound of any one of claims 1 to 14, wherein Ar² is a phenyl or 5-9 membered heteroaryl having 1-3 heteroatoms selected from N and S, each of which is optionally substituted with 1-2 R^b groups.

16. The compound of any one of claims 1 to 15, wherein Ar² is phenyl, pyridinyl, pyrimidinyl, thiazolyl, pyrazolyl, indazolyl, benzothiazolyl, benzopyrazolyl, or [1,2,4]triazolo[4,3-a]pyridinyl each of which is optionally substituted with 1-2 R^b groups.

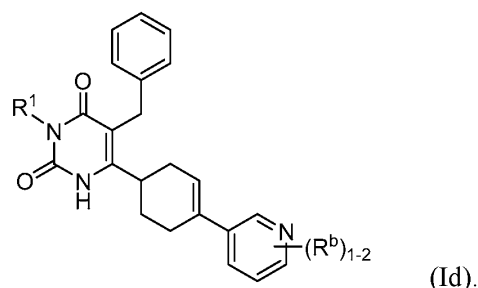
17. The compound of any one of claims 1 to 16, wherein Ar² is phenyl, which is optionally substituted with 1-2 R^b groups.

18. The compound of any one of claims 1 to 17, having formula Ic:



19. The compound of any one of claims 1 to 16, wherein Ar² is pyridin-3-yl, which is optionally substituted with 1-2 R^b groups.

20. The compound of any one of claims 1 to 16 and 19, having formula Id:



21. The compound of any one of claims 1, and 3 to 20, wherein
 each R^b is independently H, halogen, CN, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ hydroxyalkyl,
 C₁₋₄ haloalkyl, C₁₋₄ haloalkoxy, -OR^{b4}, -NR^{b1}R^{b2}, -C(O)NR^{b1}R^{b2}, -SO₂R^{b1}, -
 SO₂NR^{b1}R^{b2}, or C₃₋₆ cycloalkyl;
 R^{b1} and R^{b2} are each independently H or C₁₋₄ alkyl; or R^{b1} and R^{b2} when attached to a
 nitrogen atom are combined to form a 4-6 membered heterocycle having 1-2
 nitrogen atoms, which is optionally substituted with 1-2 R^{b3};
 each of R^{b3} is independently H, halogen, C₁₋₄ alkyl, or C₁₋₄ alkoxy; and
 each R^{b4} is independently C₁₋₄ hydroxyalkyl, C₃₋₆ cycloalkyl or C₃₋₆ cycloalkyl-C₁₋₄
 alkyl.

22. The compound of any one of claims 1 to 21, wherein
 each R^b is independently H, halogen, CN, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ hydroxyalkyl,
 C₁₋₄ haloalkyl, or C₁₋₄ haloalkoxy.

23. The compound of any one of claims 1, and 3 to 21, wherein
 each R^b is independently H, F, Cl, CN, Me, Et, nPr, iPr, nBu, iBu, sBu, tBu, OMe,
 OEt, OnPr, OiPr, CH₂F, CHF₂, CF₃, CH₂CF₃, OCH₂F, OCHF₂, OCF₃,
 OCH₂CF₃, -CH₂OH, , -OCH₂CH₂OH, -O-cyclopropyl, -O-cyclobutyl, -O-
 cyclopentyl, -O-cyclohexyl, -O-cyclopropylmethyl, -O-cyclobutylmethyl, -O-
 cyclopentylmethyl, -O-cyclohexylmethyl, -NH₂, -NHMe, -NMe₂, -SO₂Me, -
 SO₂Et, , -S(O)₂iPr, -S(O)₂NHMe, -S(O)₂NMe₂, 1-pyrrolidinyl, 1-piperidinyl,
 1-piperazinyl, -C(O)-1-pyrrolidinyl, -C(O)-1-piperidinyl, -C(O)-1-
 piperazinyl, cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl, wherein

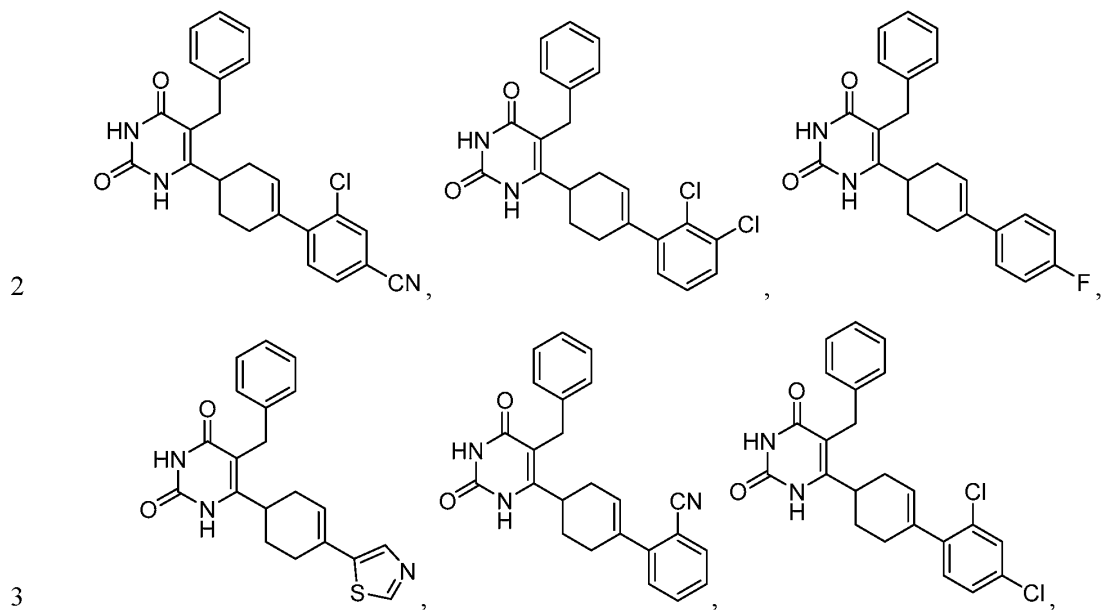
each of 1-pyrrolidinyl, 1-piperidinyl, and 1-piperazinyl is optionally substituted with
 1-2 R^{b3}; and
 each R^{b3} is independently H, F, Me, or OMe.

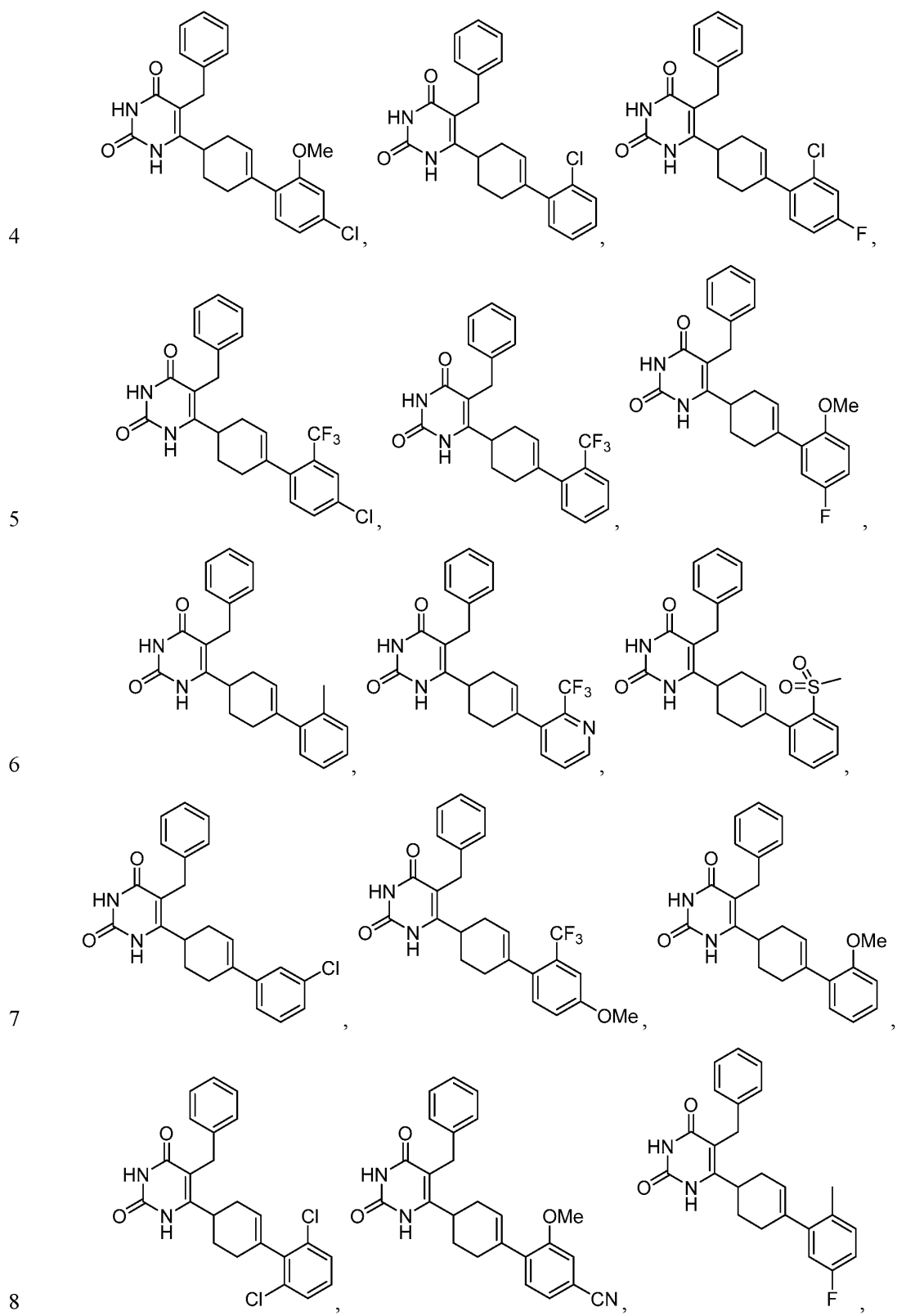
24. The compound of any one of claims 1, 3 to 21 and 23, wherein
 each R^b is independently H, F, Cl, CN, Me, Et, iBu, OMe, OEt, OiPr, CF₃, OCHF₂,
 OCF₃, OCH₂CF₃, -CH₂OH, -OCH₂CH₂OH, -O-cyclopropyl, -O-
 cyclopropylmethyl, -NMe₂, -S(O)₂Me, -S(O)₂Et, -S(O)₂iPr, -S(O)₂NHMe, -
 S(O)₂NMe₂, 1-pyrrolidinyl, 1-piperidinyl, 4,4-difluoro-1-piperidinyl, 3,3-
 dimethyl-1-piperidinyl, 3-methyl-1-piperidinyl, 3-methoxy-1-piperidinyl, -
 C(O)-1-pyrrolidinyl, -C(O)-4-methyl-1-piperazinyl, or cyclopropyl.

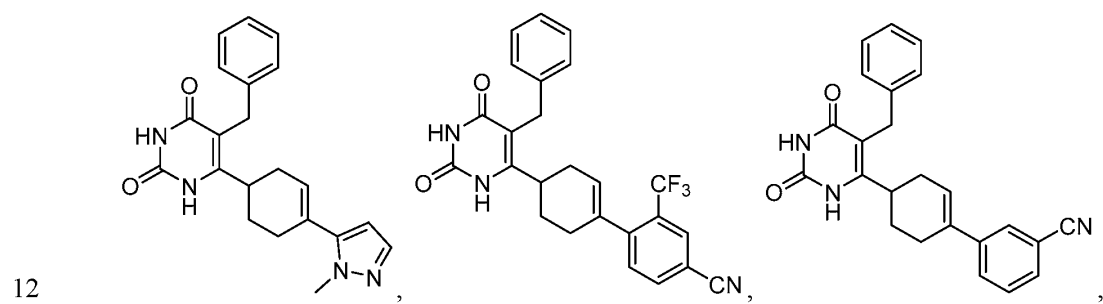
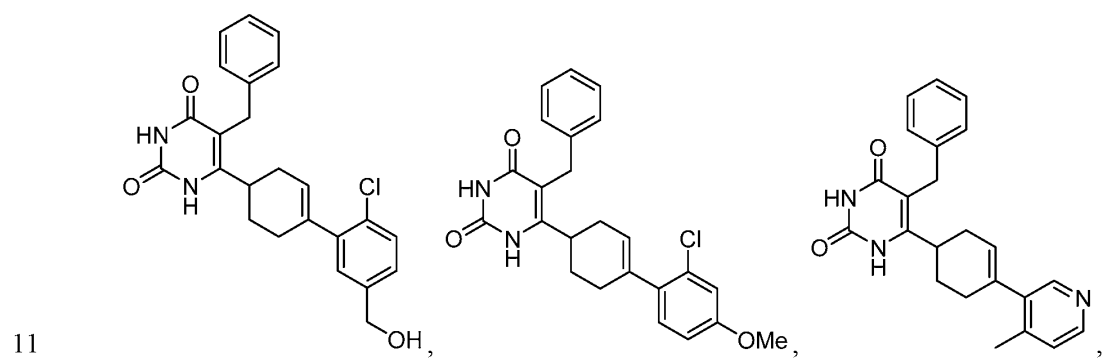
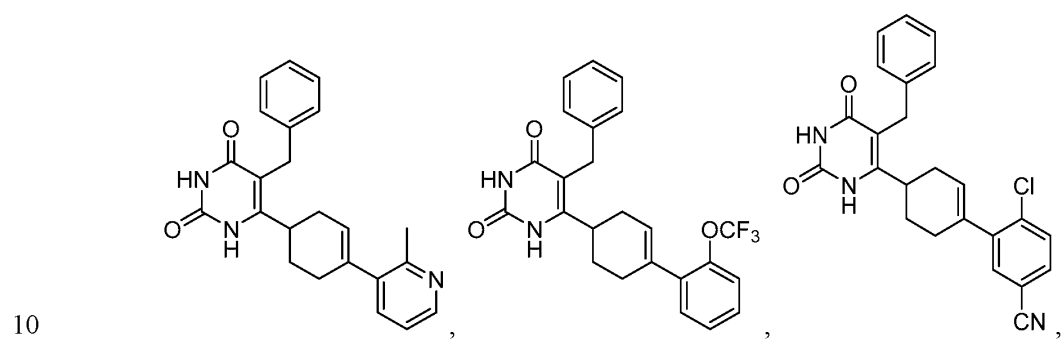
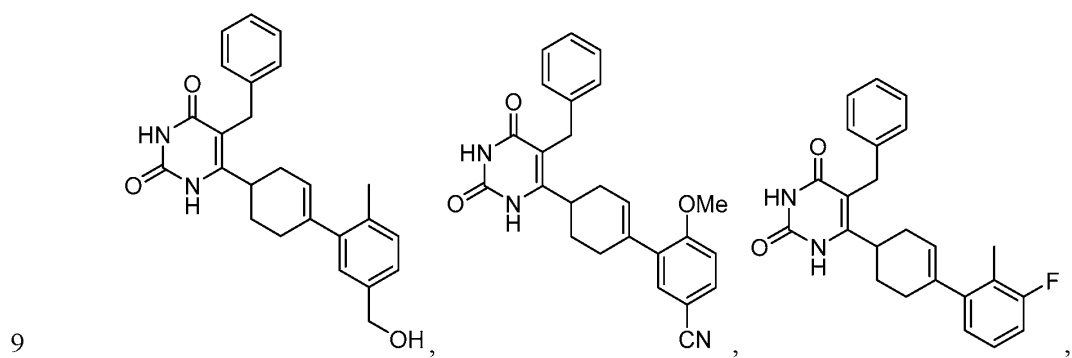
25. The compound of any one of claims 1 to 24, wherein each R^b is
 independently H, F, Cl, CN, Me, CF₃, OCF₃, or -CH₂OH.

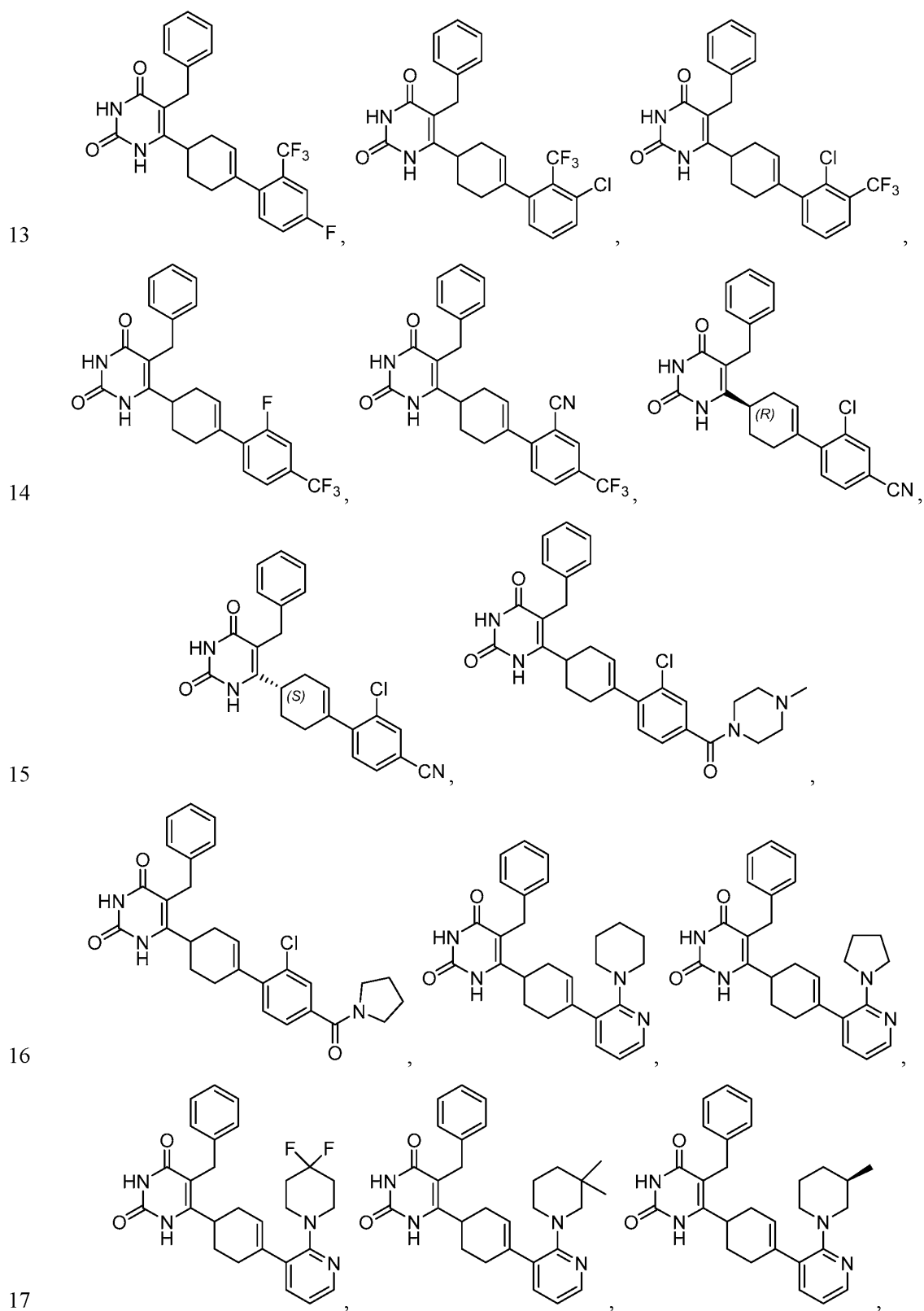
26. The compound of any one of claims 1 to 25, wherein R¹ is H.

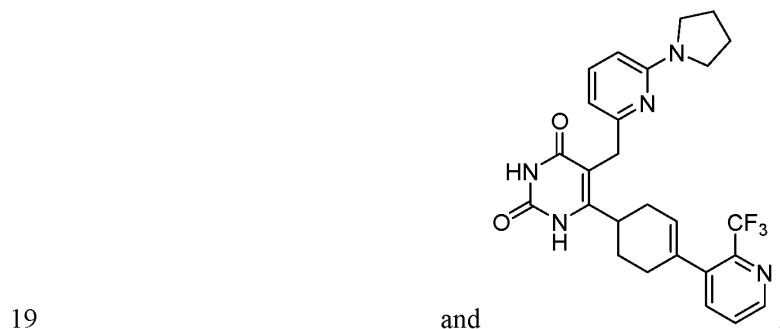
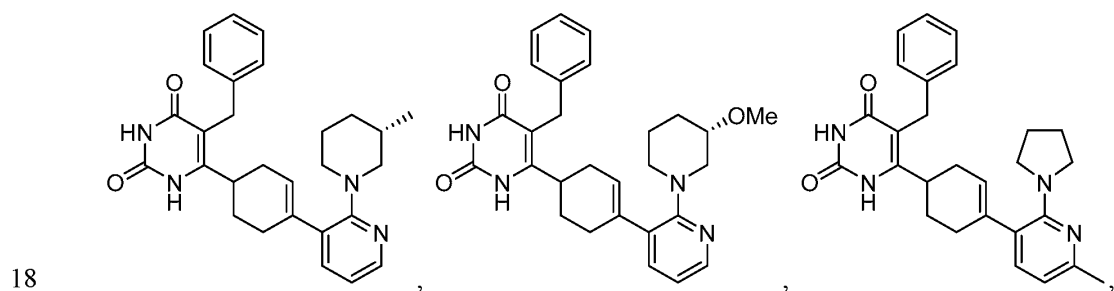
27. The compound of claim 1, selected from the group consisting of:



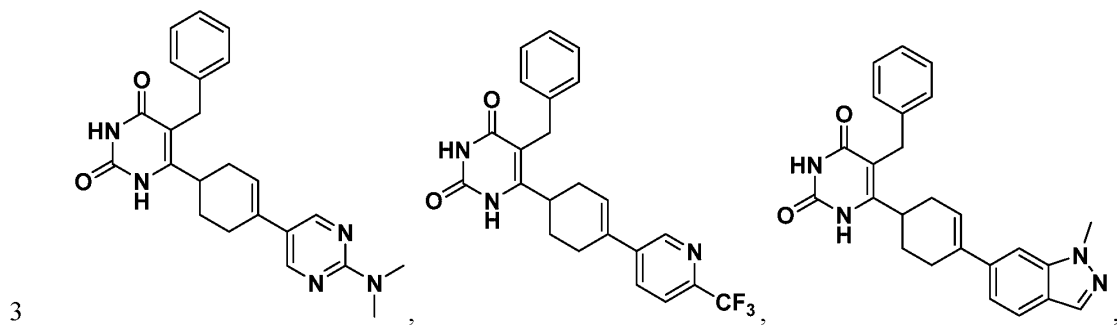
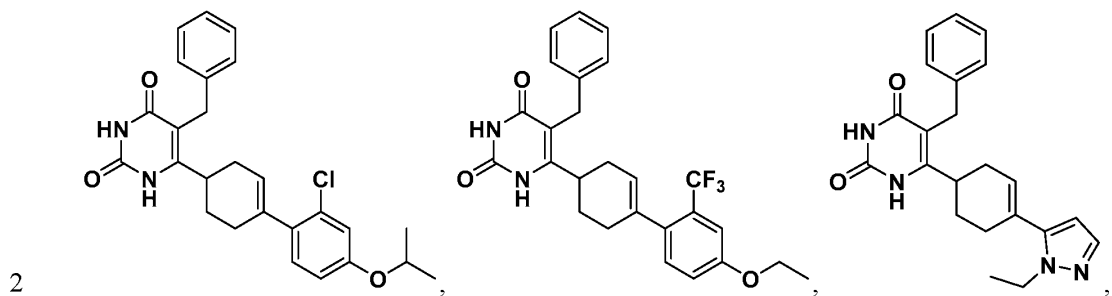


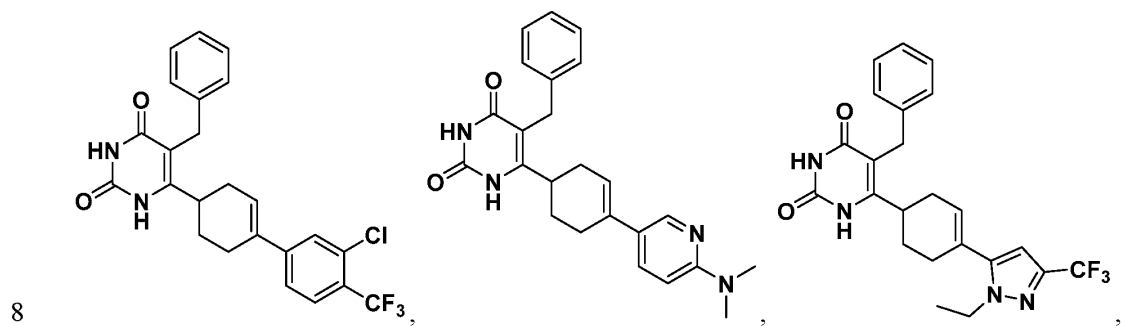
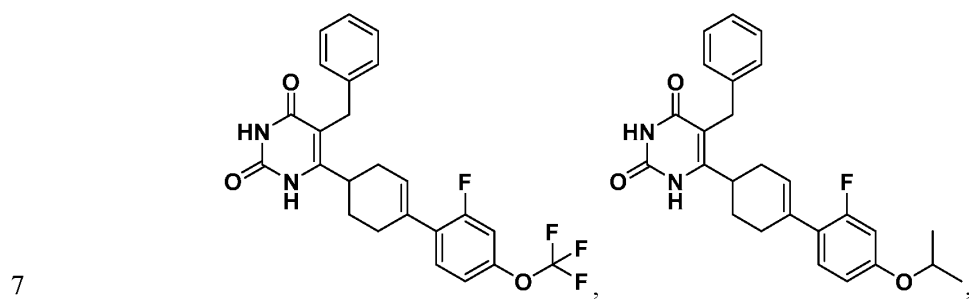
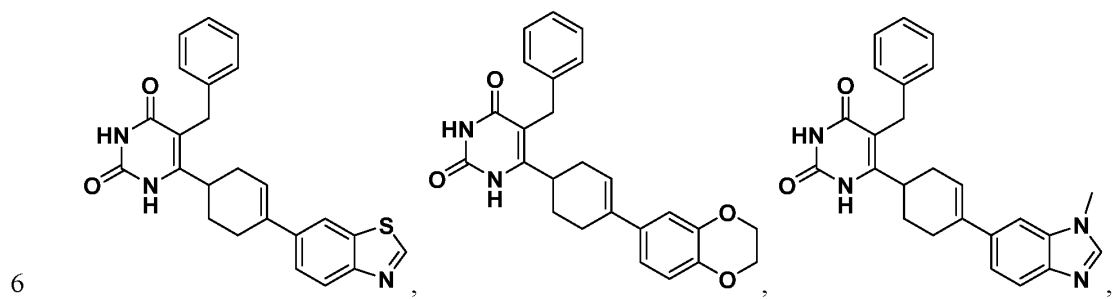
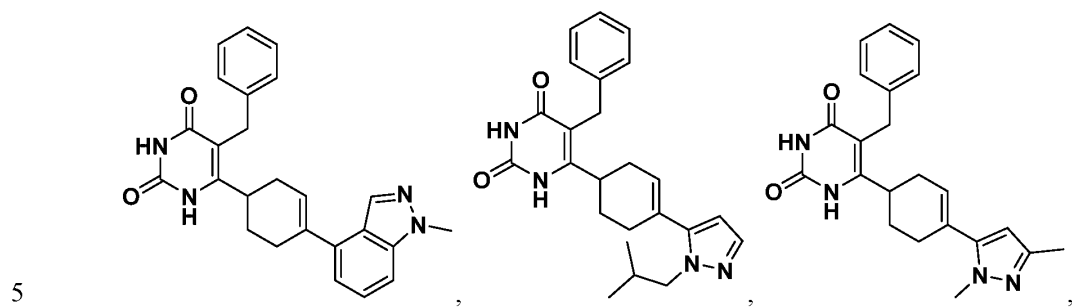
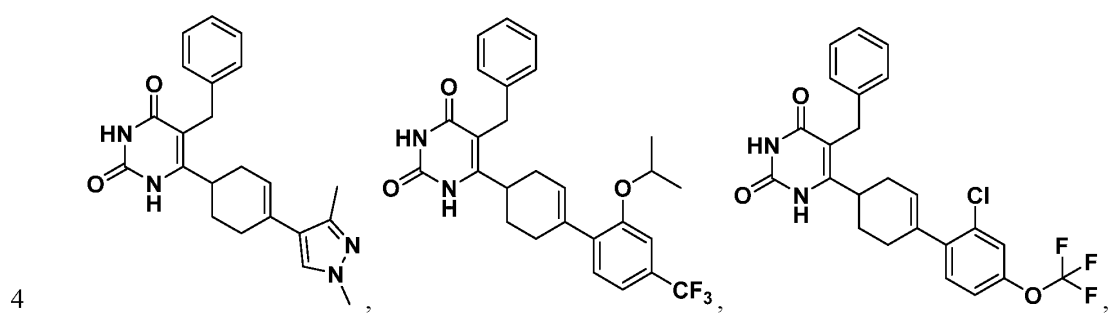


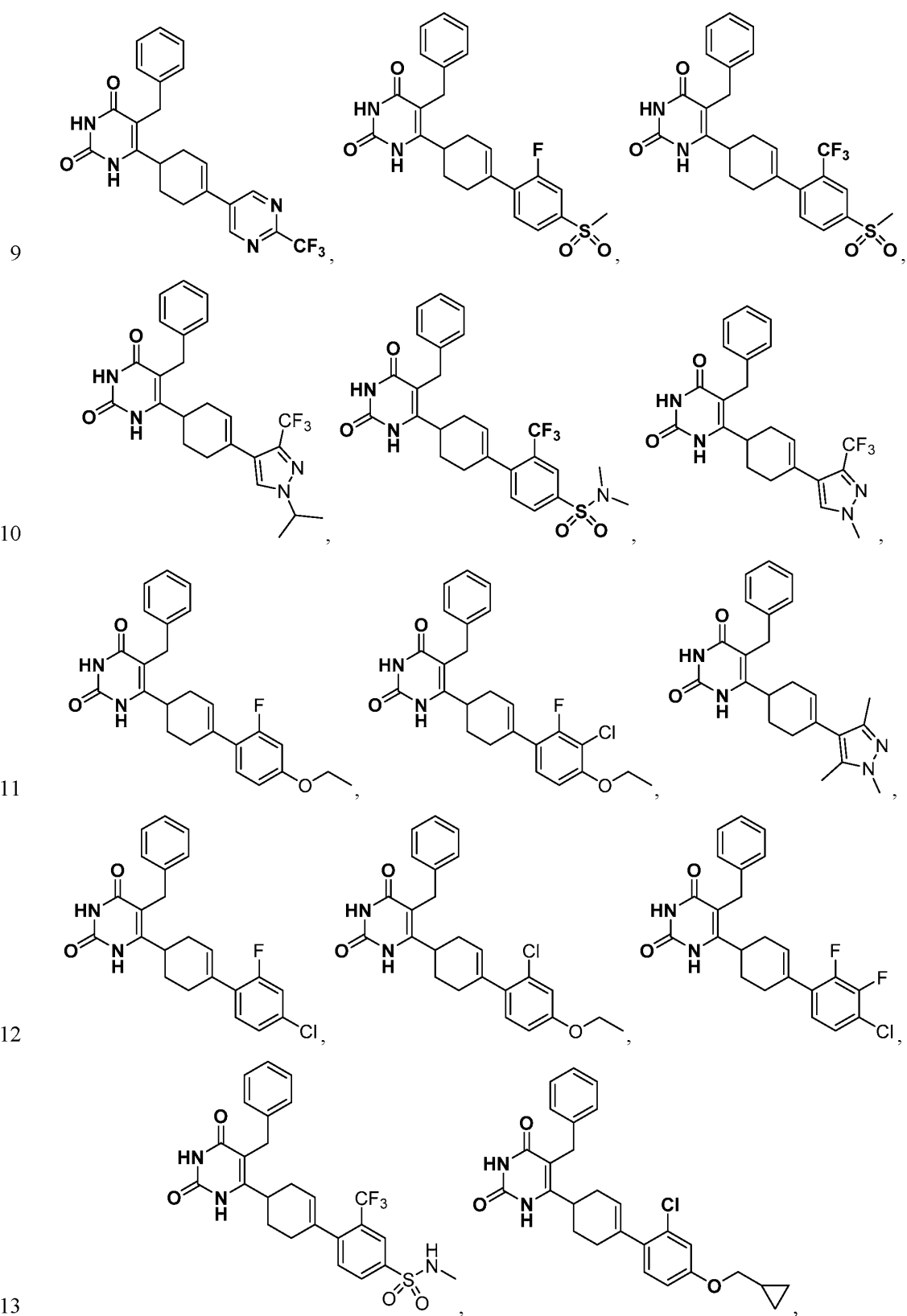


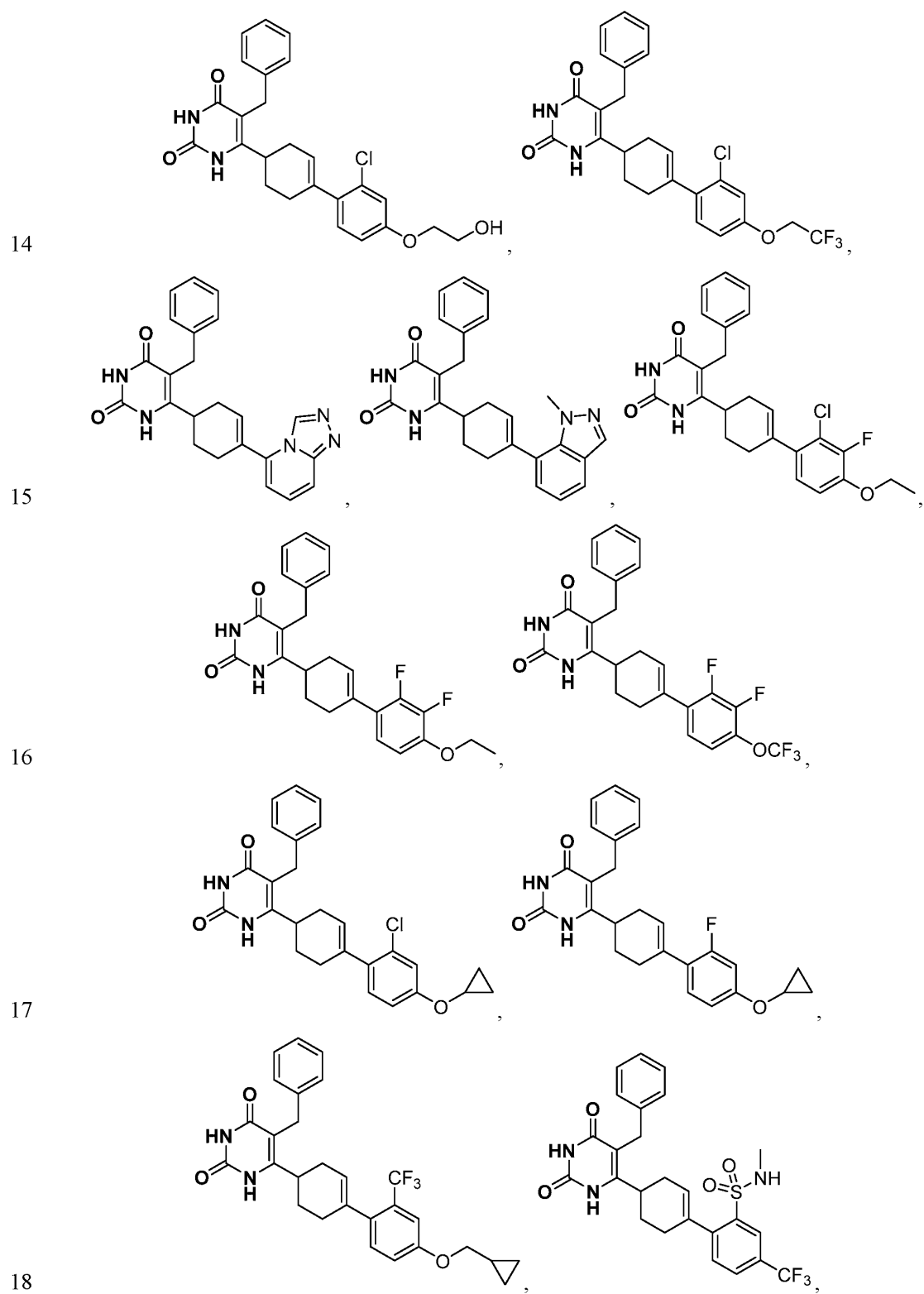


1 28. The compound of claim 1, selected from the group consisting of:

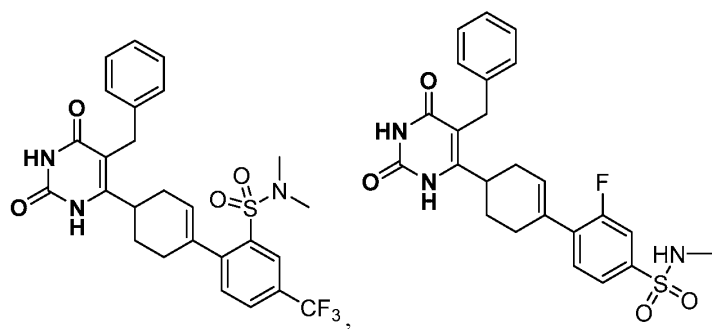




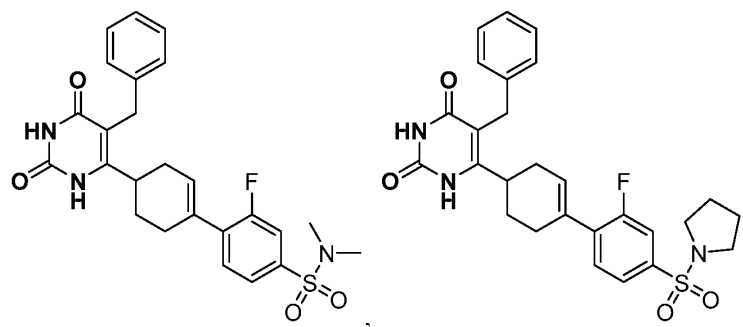




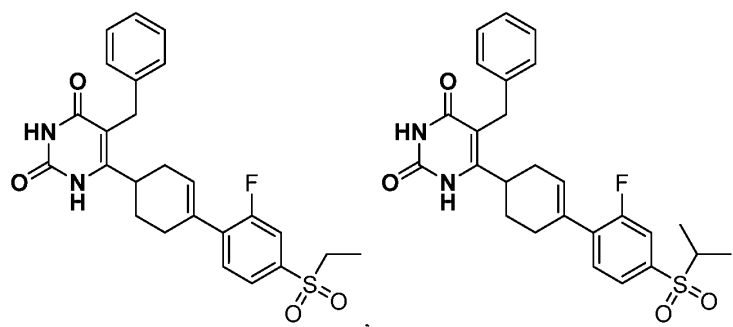
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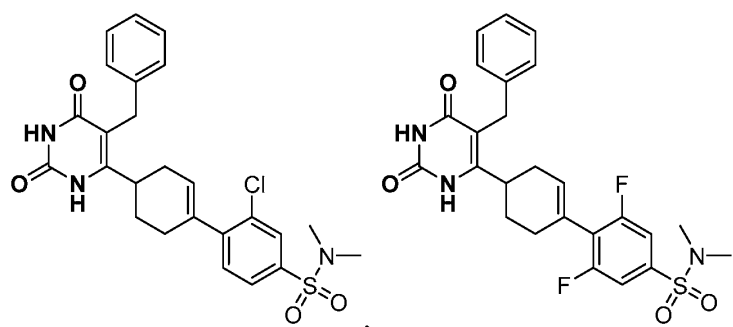
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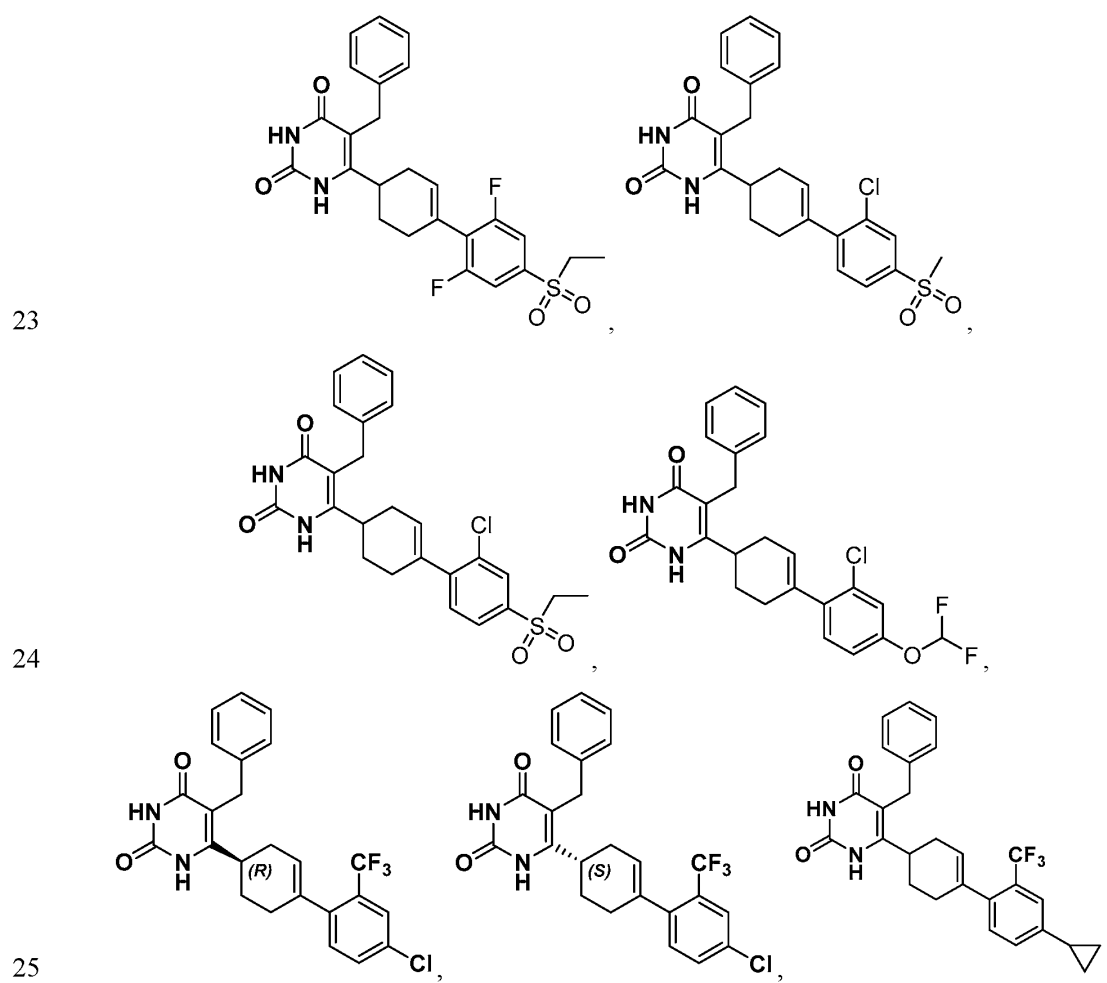


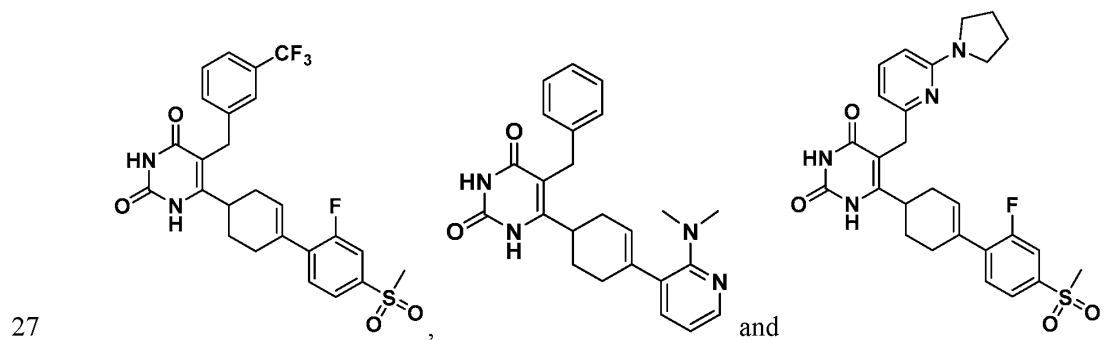
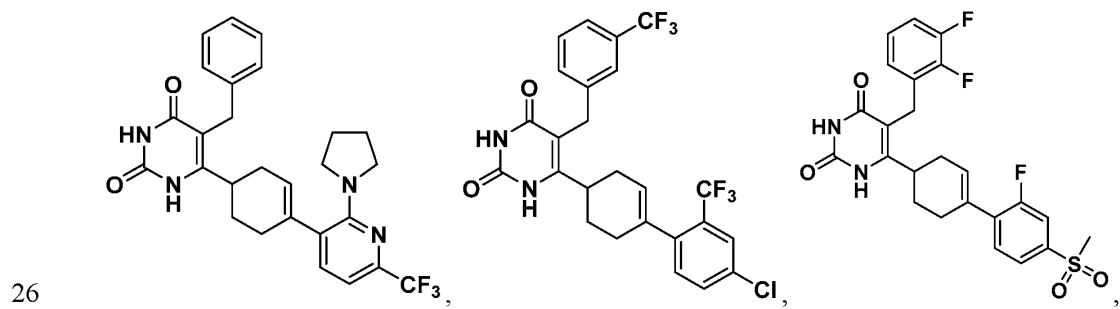
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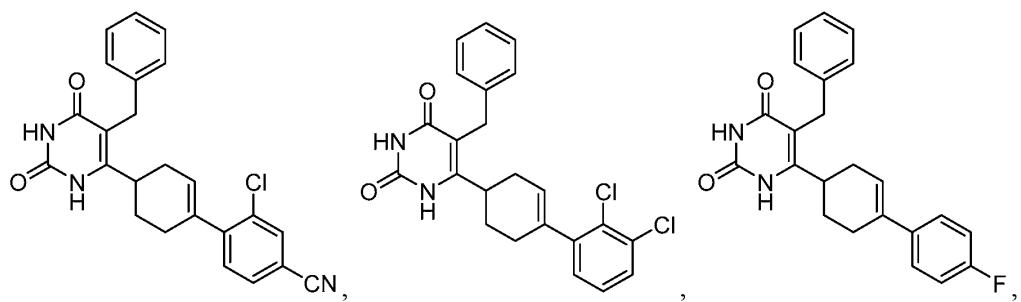




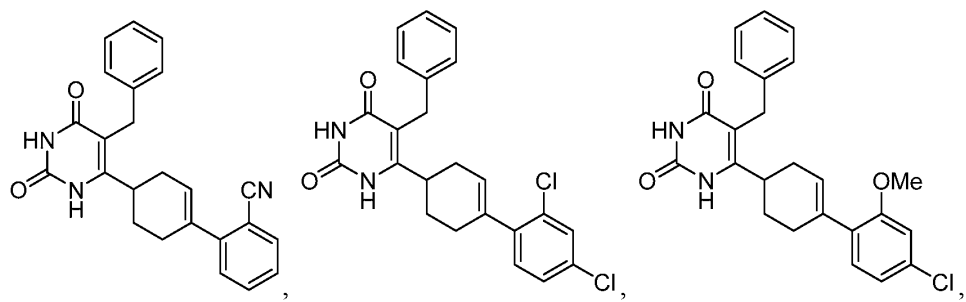
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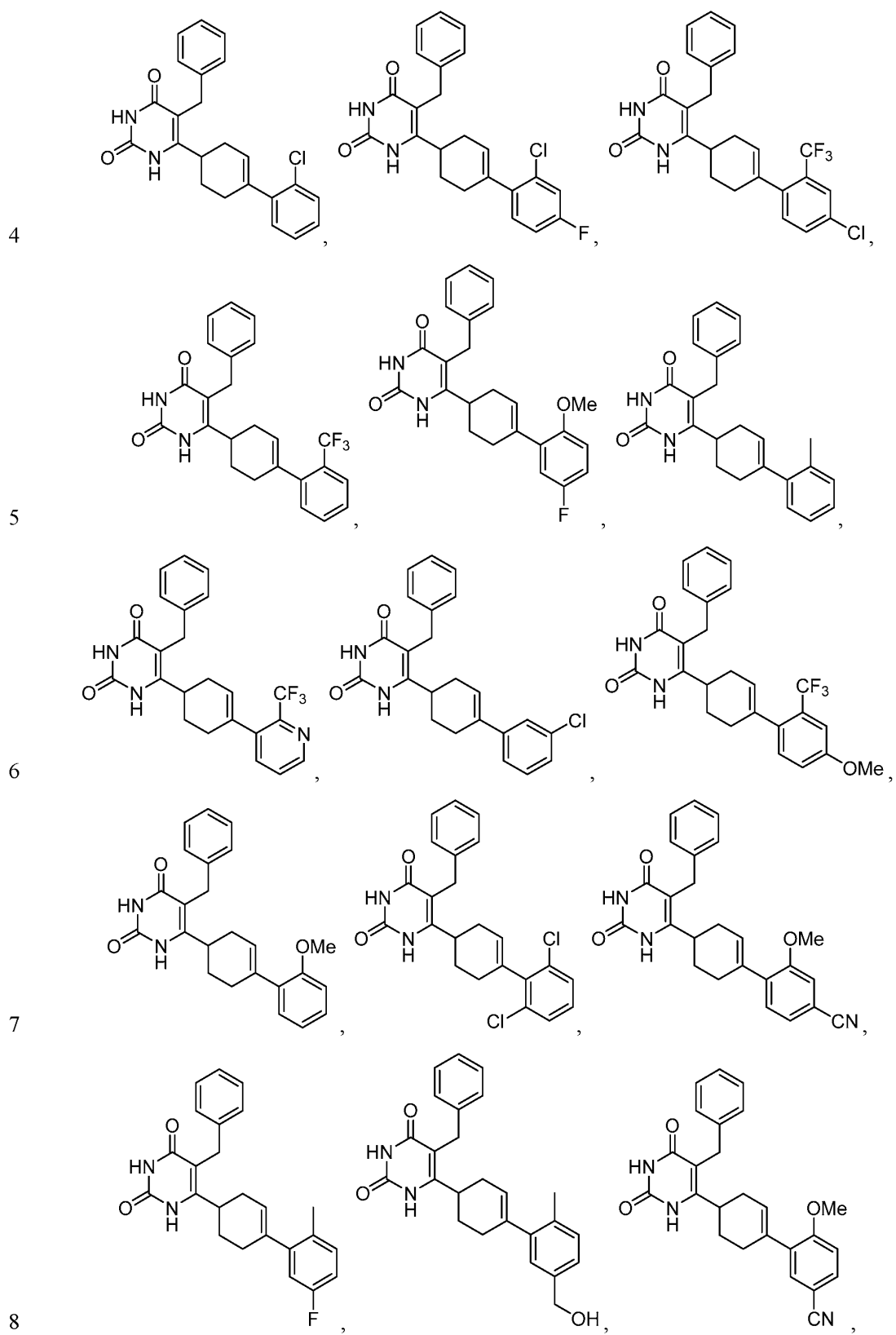
29. The compound of claim 1, selected from the group consisting of:

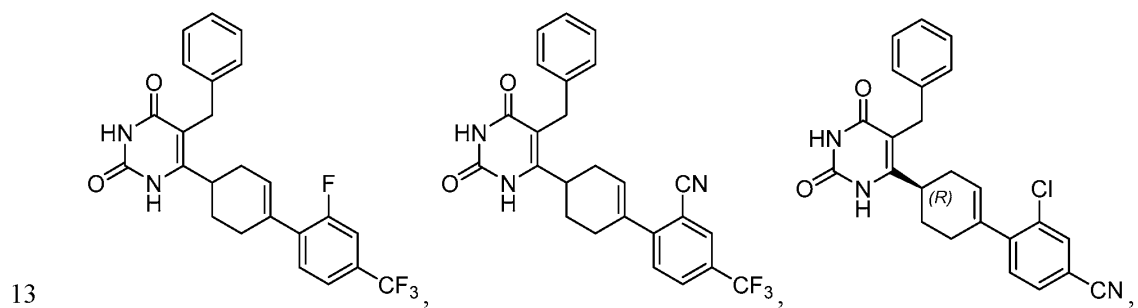
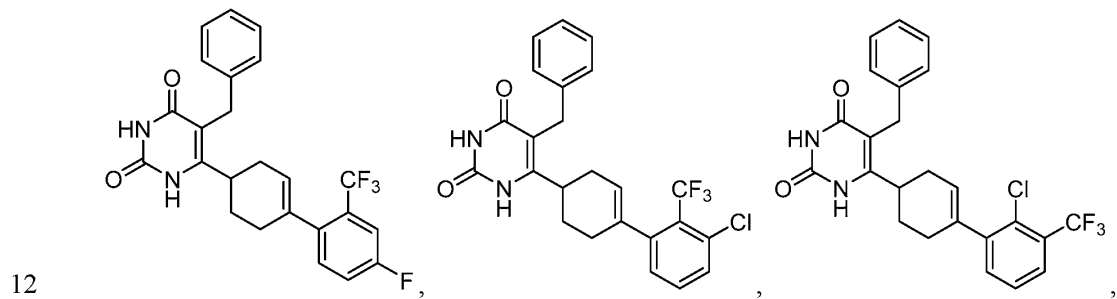
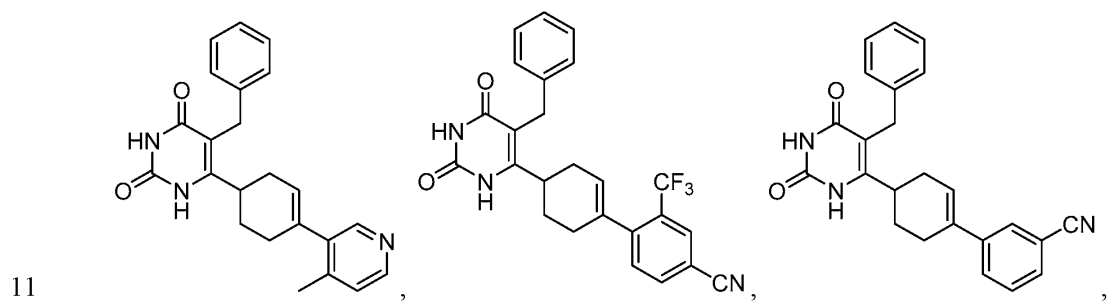
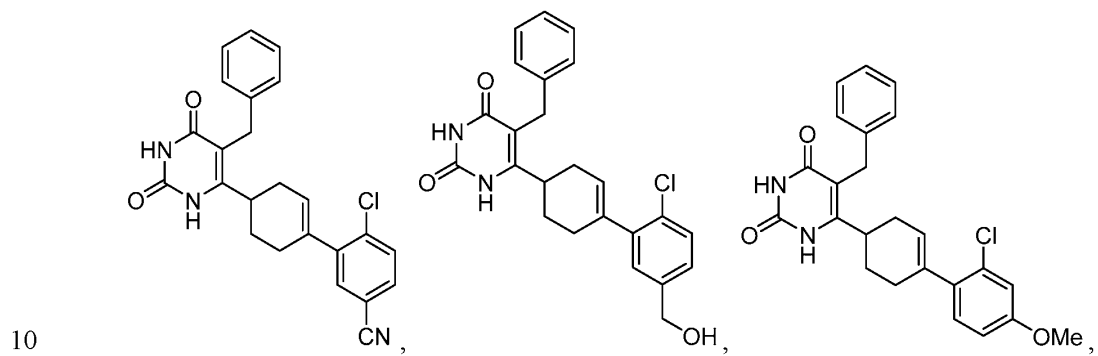
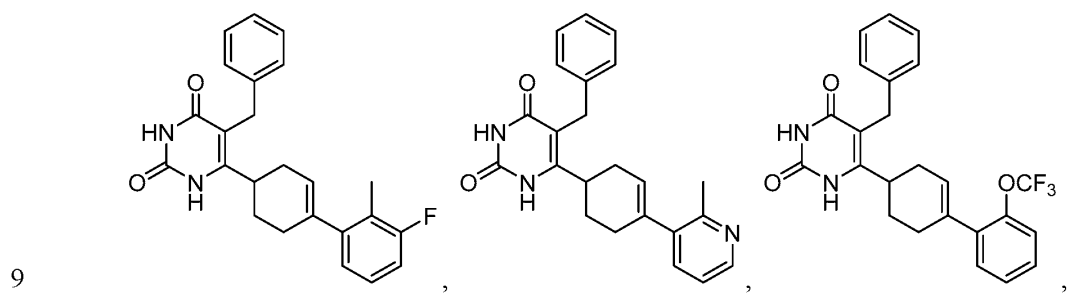
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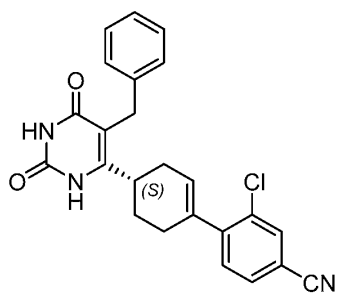


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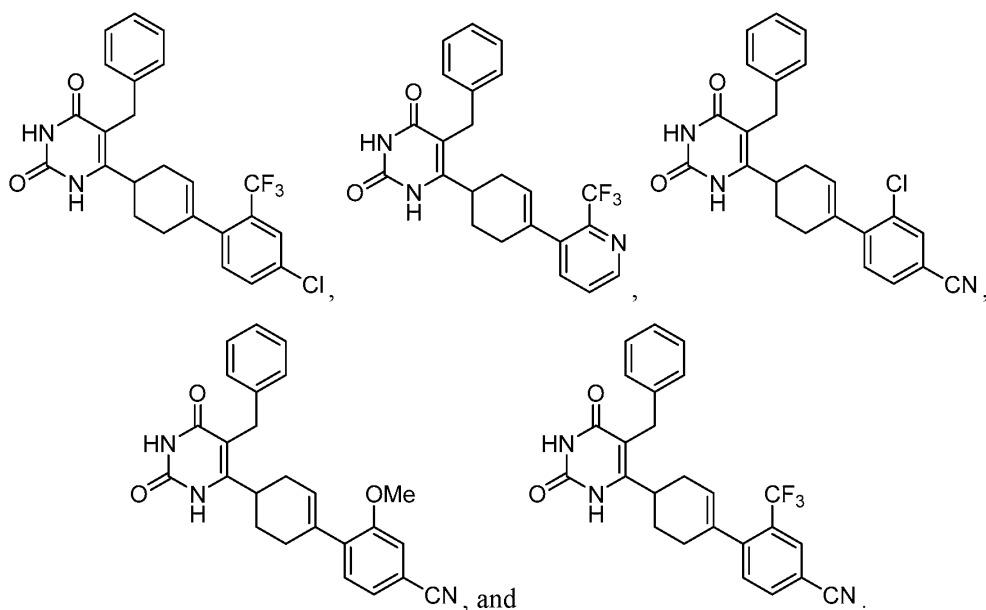


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30. The compound of claim 27, selected from the group consisting of:

2



3

1

31. A pharmaceutical composition comprising one or more

2

pharmaceutically acceptable excipients and a compound of any one of claims 1 to 30.

1

32. A method of treating a disorder or condition through modulating a

2

glucocorticoid receptor, the method comprising administering to a subject in need of such

3

treatment, a therapeutically effective amount of a compound of any one of claims 1 to 30 or a

4

pharmaceutical composition of claim 31, thereby treating the disorder or condition.

1

33. A method of treating a disorder or condition through antagonizing a

2

glucocorticoid receptor, the method comprising administering to a subject in need of such

3

treatment, an effective amount of the compound of any of claims 1 to 30 or a pharmaceutical

4

composition of claim 31.

1 34. The method of claim 33, wherein the disorder or condition is selected
2 from the group consisting of obesity, diabetes, cardiovascular disease, hypertension,
3 Syndrome X, depression, anxiety, glaucoma, human immunodeficiency virus (HIV) or
4 acquired immunodeficiency syndrome (AIDS), neurodegeneration, Alzheimer's disease,
5 Parkinson's disease, cognition enhancement, Cushing's Syndrome, Addison's Disease,
6 osteoporosis, frailty, muscle frailty, inflammatory diseases, osteoarthritis, rheumatoid
7 arthritis, asthma and rhinitis, adrenal function-related ailments, viral infection,
8 immunodeficiency, immunomodulation, autoimmune diseases, allergies, wound healing,
9 compulsive behavior, multi-drug resistance, addiction, psychosis, anorexia, cachexia, post-
10 traumatic stress syndrome, post-surgical bone fracture, medical catabolism, major psychotic
11 depression, mild cognitive impairment, psychosis, dementia, hyperglycemia, stress disorders,
12 antipsychotic induced weight gain, delirium, cognitive impairment in depressed patients,
13 cognitive deterioration in individuals with Down's syndrome, psychosis associated with
14 interferon-alpha therapy, chronic pain, pain associated with gastroesophageal reflux disease,
15 postpartum psychosis, postpartum depression, neurological disorders in premature infants,
16 and migraine headaches.

1 35. The method of claim 33, wherein the disorder or condition is
2 nonalcoholic fatty liver disease and/or nonalcoholic steatohepatitis.

1 36. The method of claim 33, wherein the disorder or condition is an
2 addiction disorder.

1 37. The method of claim 33, wherein the disorder or condition is cancer.