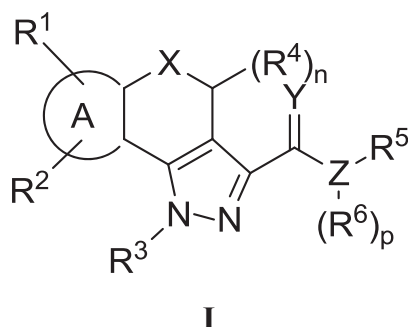


CLAIMS

We claim:

1. A compound of formula **I**,



or a pharmaceutically acceptable salt thereof, wherein:

X is O, S, SO, SO₂, or NR;

Y is O, S, or NR;

Z is O, S, SO, SO₂, or N; wherein when Z is O, S, SO, or SO₂, then p is 0;

each R is independently hydrogen, C₁₋₆ aliphatic, C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted; or

two R groups on the same atom are taken together with the atom to which they are attached to form a C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted;

Ring A is a fused C₃₋₁₀ aryl, a fused 3-8 membered saturated or partially unsaturated carbocyclic ring, a fused 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a fused 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

R¹ is -OR, -SR, -CN, -NO₂, -SO₂R, -SOR, -C(O)R, -CO₂R, -C(O)N(R)₂, -NRC(O)R, -NRC(O)N(R)₂, -NRSO₂R, or -N(R)₂;

R² is -R, halogen, -haloalkyl, -OR, -SR, -CN, -NO₂, -SO₂R, -SOR, -C(O)R, -CO₂R, -C(O)N(R)₂, -NRC(O)R, -NRC(O)N(R)₂, -NRSO₂R, or -N(R)₂;

R³ is hydrogen, C₁₋₆ aliphatic, C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted;

each R⁴ is independently -R, halogen, -haloalkyl, -OR, -SR, -CN, -NO₂, -SO₂R, -SOR, -C(O)R, -CO₂R, -C(O)N(R)₂, -NRC(O)R, -NRC(O)N(R)₂, -NRSO₂R, or -N(R)₂;

R⁵ is C₁₋₆ aliphatic, C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted;

R⁶ is hydrogen, C₁₋₆ aliphatic, C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted;

or R⁵ and R⁶, together with the atom to which each is attached, form a 3-8 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 3-8 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted;

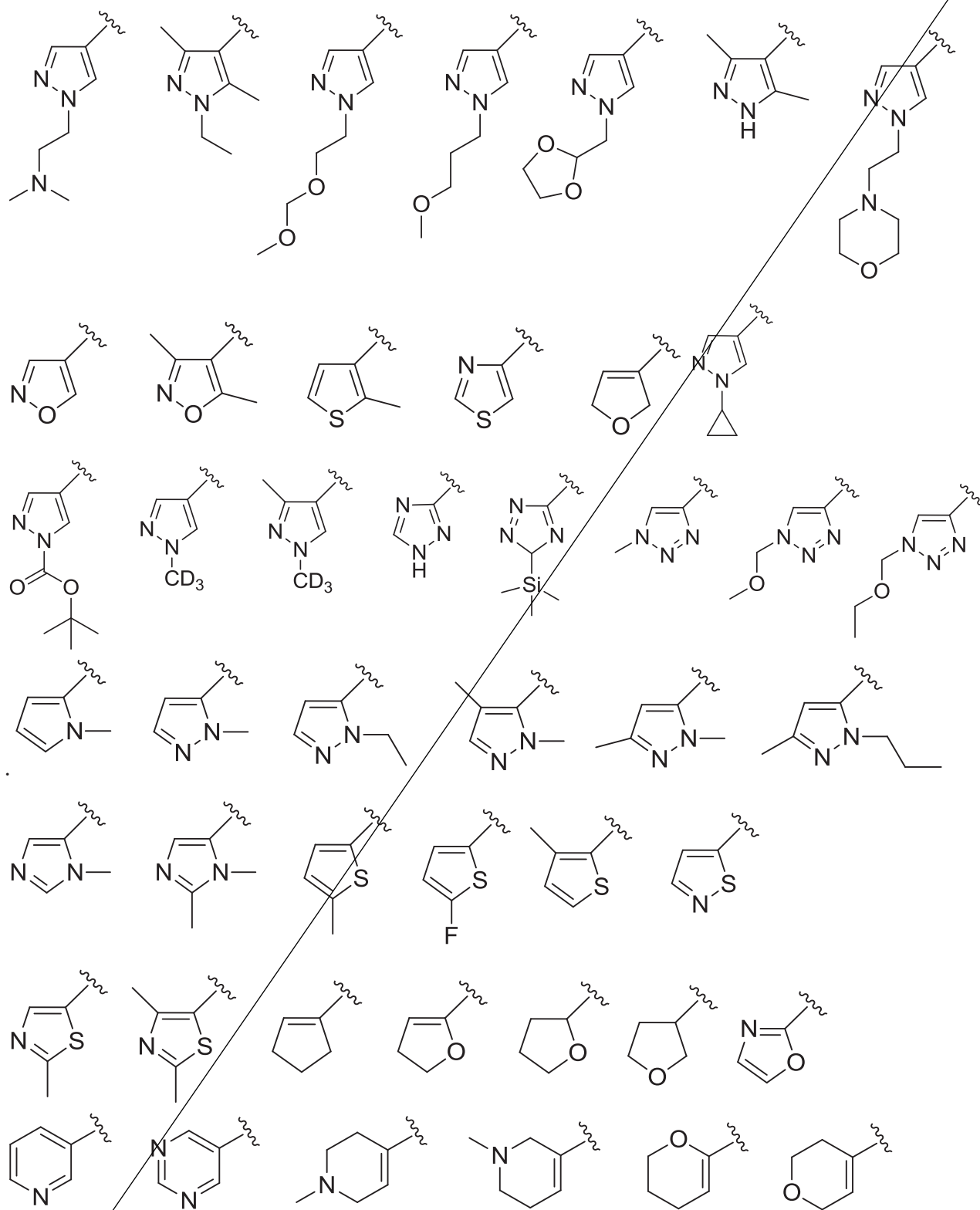
n is 0, 1, or 2; and

p is 0 or 1.

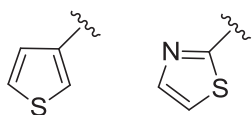
2. The compound of claim 1, wherein X is O.

3. The compound of claim 1, wherein Y is O.

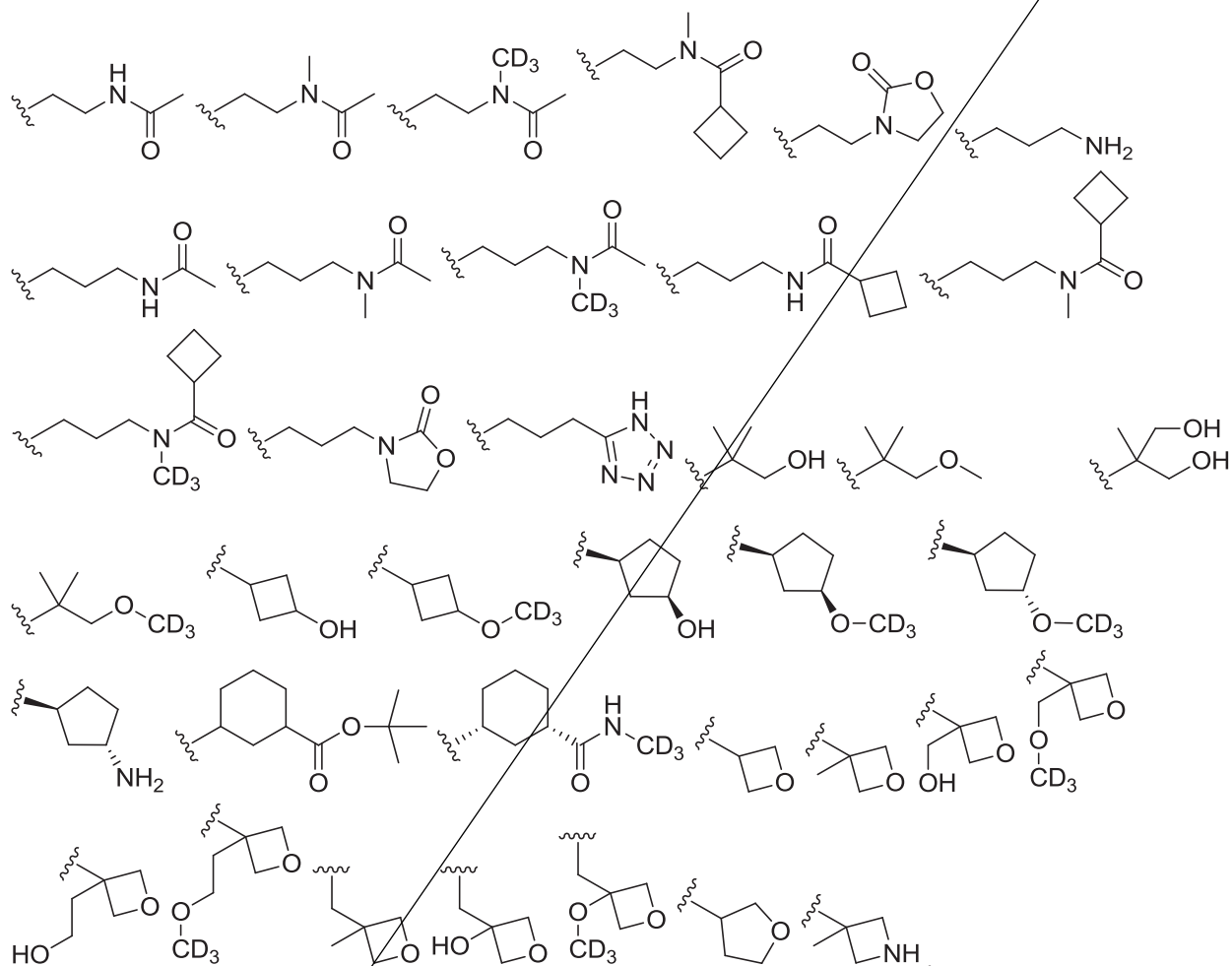
4. The compound of claim 1, wherein Z is N.



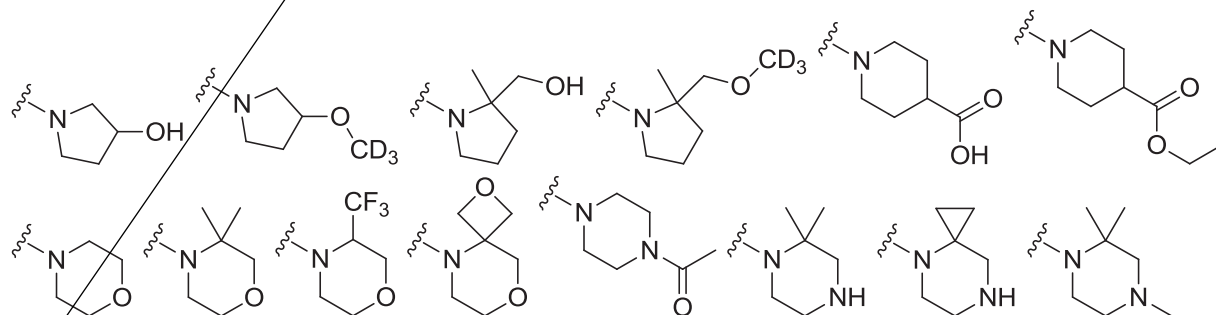
8. The compound of claim 14, wherein R^3 is

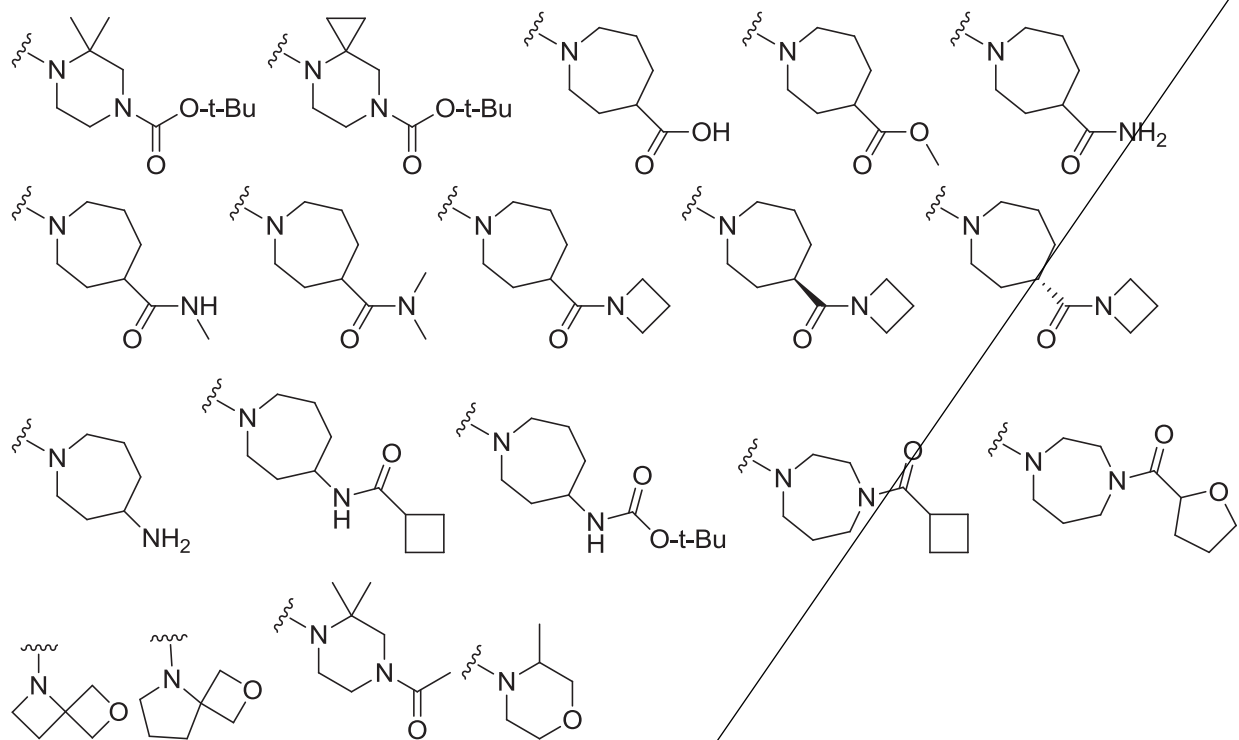


9. The compound of claim 1, wherein R^5 is methyl, t-butyl, $-CD_3$,

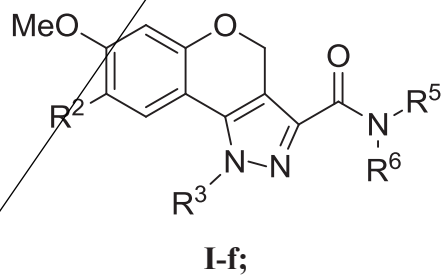


10. The compound of claim 1, wherein Z is N and the ring formed by Z, R^5 and R^6 is



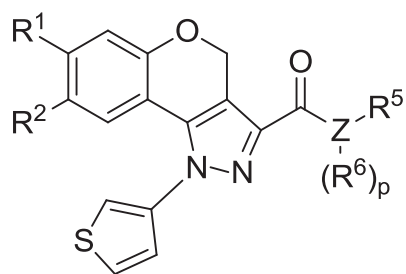


11. The compound of claim 1, wherein R^6 is hydrogen, methyl, t-butyl, or $-CD_3$.
12. The compound of claim 1, of formula **I-f**:



or a pharmaceutically acceptable salt thereof.

13. The compound of claim 1, of formula **I-h**:



I-h;

or a pharmaceutically acceptable salt thereof.

14. The compound of claim 1, selected from Table 1.

15. A pharmaceutical composition comprising a compound of claim 1, and a pharmaceutically acceptable adjuvant, carrier, or vehicle.

16. A method for modulating FSHR, or a mutant thereof, activity in a patient or in a biological sample, comprising the step of administering to said patient or contacting said biological sample with a compound of claim 1 or a physiologically acceptable salt thereof.

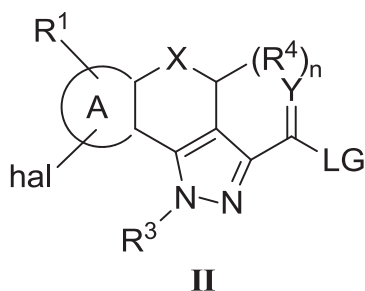
17. A method for treating a FSHR-mediated disorder in a patient in need thereof, comprising the step of administering to said patient a compound of claim 1.

18. A method for treating fertility disorders in a subject, comprising the step of administering to said subject a compound of claim 1 or a physiologically acceptable salt thereof.

19. Use of a compound according to claim 1 or physiologically acceptable salts thereof, for the production of a medicament for the prophylactic or therapeutic treatment of a FSHR-mediated disorder.

20. A process for manufacturing a compound of formula I according to claim 1, comprising the steps of:

reacting a compound of formula (II)

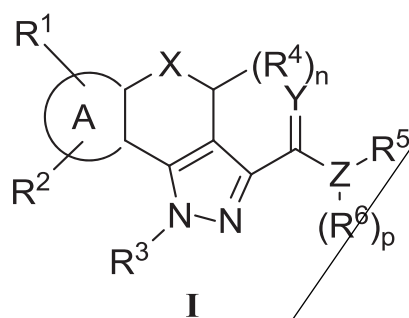


wherein X, Y, R¹, R³, R⁴, and n are as defined in claim 1, and LG is a leaving group;

with a compound of formula ZH(R⁵)(R⁶)_p

wherein Z, R⁵, R⁶, and p are as defined in claim 1;

to yield a compound of formula **I**:

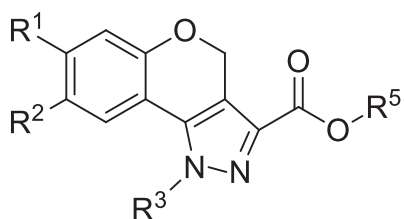


wherein X, Y, Z, R¹, R², R³, R⁴, R⁵, R⁶, n, and p, are as defined in claim 1.

Claims

We claim:

1. A method of modulating FSHR, or a mutant thereof, activity in a patient or in a biological sample, comprising the step of administering to said patient or contacting said biological sample with a compound of formula I-e:

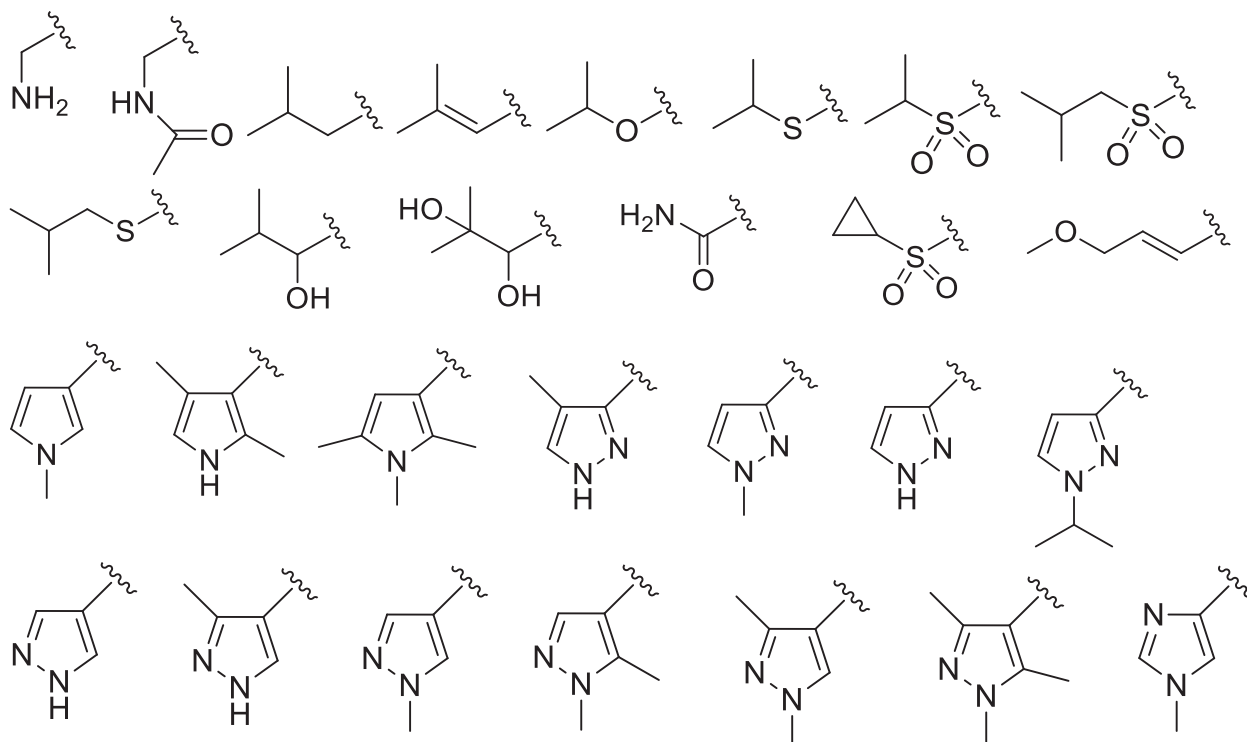


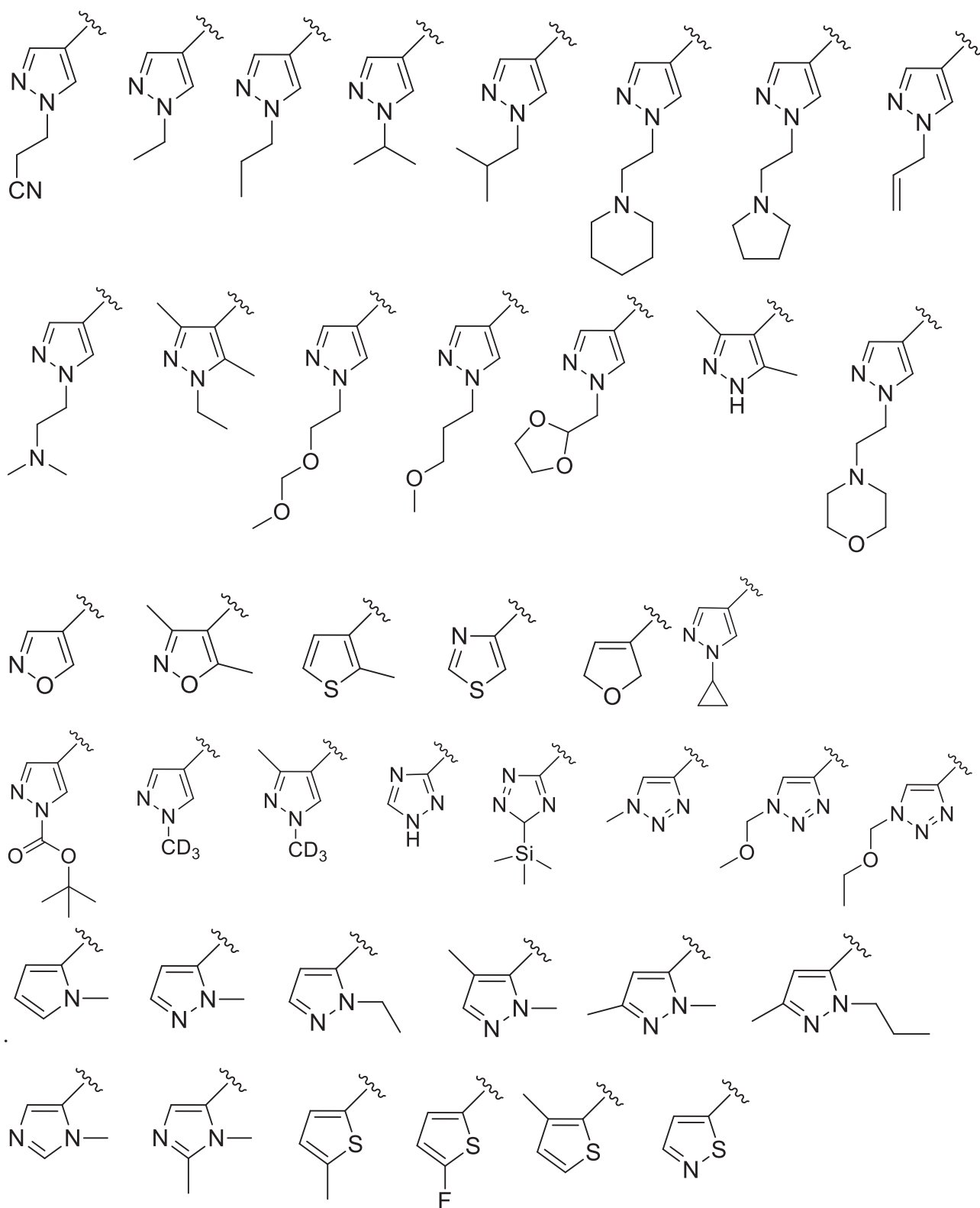
I-e;

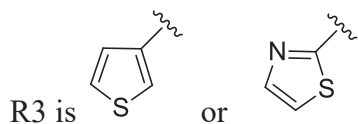
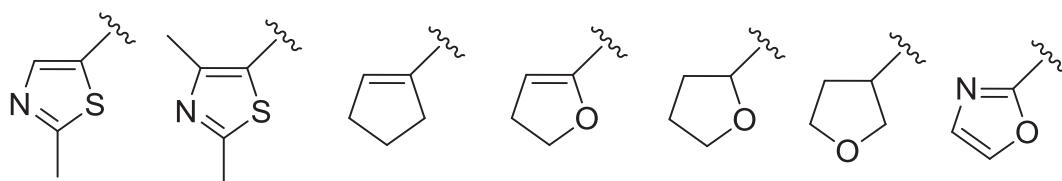
or a pharmaceutically acceptable salt thereof, wherein:

R¹ is -OR, wherein said R of -OR is C₁₋₆ aliphatic;

R² is Br, CN,







and

R5 is methyl, t-butyl, -CD₃,

