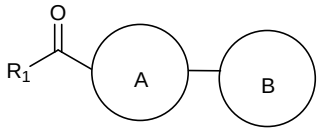
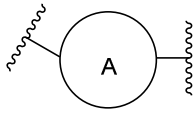
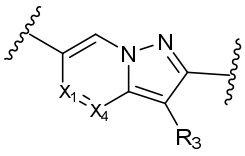
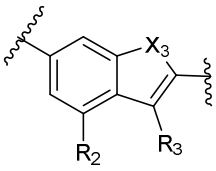
CLAIMS

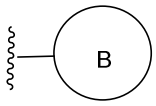
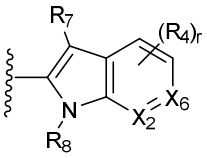
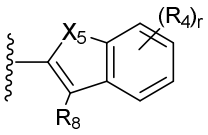
1. A compound of Formula (Ia):



(Ia)

or a pharmaceutically acceptable salt thereof, wherein:

 is selected from  and  ;

 is selected from  and  ;

X_1 is independently selected from CR_2, and N;

X_2 is independently selected from CR_4, and N;

X_3 is independently selected from O, and S;

X_4 is independently selected from CR_2, and N; provided X_1 and X_4 are not both N;

X_5 is independently selected from O and S;

X_6 is independently selected from CR_4, and N; provided 1) X_2 and X_6 are not both N; 2) when X_2 and X_6 are both CR_4, one of R_4 is H;

R_1 is independently selected from –NH-C_{1-5} alkyl optionally substituted with one or more substituents selected from F, Cl, and NH_2, 4-10 membered heterocyclyl, and –NH–4-10 membered heterocyclyl, wherein said heterocyclyl is optionally substituted with one or more substituents selected from F, Cl, CN, C_{1-3} alkyl, =N-OR_b, -$(CH_2)_rOR_b$, -$(CH_2)_rNR_aR_a$, -$NR_aC(=NH)C_{1-3}$ alkyl, -$NR_aC(=O)OR_b$, carbocyclyl, and heterocyclyl;

R_2 is independently selected from H, F, Cl, C_{1-4} alkyl optionally substituted with one or more substituents selected from F, Cl, and OH, and –OC_{1-4} alkyl;

R_3 is independently selected from H, F, Cl, CN, –C(=O)OR_b, and C_{1-3} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, NH_2, and N_3;

R_4 is independently selected from H, F, Cl, Br, -C(=O)R_b, C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –NH-C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –$(CH_2)_r$–aryl substituted with one or more R_5, -O-C_{1-6} alkyl substituted with one or more R_5, –$(CH_2)_r$–C_{3-12} cycloalkyl substituted with one or more R_5, and –$(CH_2)_r$–4–10 membered heterocyclyl comprising carbon atoms and 1–5 heteroatoms selected from N, NR_6, O, and S and substituted with one or more R_5;

R_5 is independently selected from H, F, Cl, Br, CN, =O, C_{1-4} alkyl optionally substituted with one or more R_e, C_{2-4} alkenyl optionally substituted with one or more R_e, C_{2-4} alkynyl optionally substituted with one or more R_e, –$(CR_dR_d)_rOR_b$, –$(CR_dR_d)_rS(O)_pR_c$, –$(CR_dR_d)_rS(O)_pNR_aR_a$, –$(CR_dR_d)_rNR_aS(O)_pR_c$, –$(CR_dR_d)_rNR_aR_a$, –$(CR_dR_d)_rNR_aC(=O)R_b$, –$(CR_dR_d)_rNR_aC(=O)OR_b$, –$(CR_dR_d)_rNR_aC(=O)NR_aR_a$, –$(CR_dR_d)_rC(=O)R_b$, –$(CR_dR_d)_rC(=O)OR_b$, –$(CR_dR_d)_rC(=O)NR_aR_a$, –$(CR_dR_d)_rOC(=O)R_b$, –$(CR_dR_d)_rOC(=O)OR_b$, –$(CR_dR_d)_rO(CH_2)_rC(=O)NR_aR_a$, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_6 is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, -$S(O)_pR_c$, -$S(O)_pNR_aR_a$, -C(=O)R_b, –C(=O)OR_b, -C(=O)NR_aR_a, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_7 is independently selected from H, F, and Cl;

R_8 is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, and C_{3-6} cycloalkyl;

R_a is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more R_e, C_{2-6} alkynyl optionally substituted with one or more R_e, –$(CH_2)_r$–C_{3-10} carbocyclyl optionally substituted with one or more R_e, and –$(CH_2)_r$–heterocyclyl optionally substituted with one or more R_e; or R_a and R_a together with the nitrogen atom to which they are both attached form a heterocyclic ring optionally substituted with one or more R_e;

R_b is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more R_e, C_{2-6} alkynyl optionally

substituted with one or more R_e, $-(CH_2)_r-C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $-(CH_2)_r$-heterocyclyl optionally substituted with one or more R_e;

R_c is independently selected from C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more R_e, C_{2-6} alkynyl optionally substituted with one or more R_e, $-(CH_2)_r-C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $-(CH_2)_r-$heterocyclyl optionally substituted with one or more R_e;

R_d is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more R_e;

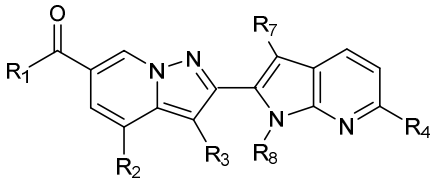
R_e is independently selected from F, Cl, Br, CN, NH_2, $-NH-C_{1-4}$ alkyl, $-N(C_{1-4}$ alkyl$)_2$, =O, OH, $-OC_{1-6}$ alkyl, $-CO_2H$, C_{1-6} alkyl optionally substituted with one or more R_f, C_{2-6} alkenyl, C_{2-6} alkynyl, $-(CH_2)_r-C_{3-6}$ cycloalkyl optionally substituted with one or more R_f, $-(CH_2)_r-$aryl optionally substituted with one or more R_f, and $-(CH_2)_r-$heterocyclyl optionally substituted with one or more R_f;

R_f is independently selected from F, Cl, Br, CN, OH, OC_{1-5} alkyl, C_{1-5} alkyl optionally substituted with OH, C_{2-5} alkenyl, C_{2-5} alkynyl, C_{3-6} cycloalkyl, and phenyl;

p, at each occurrence, is independently selected from zero, 1, and 2; and

r, at each occurrence, is independently selected from zero, 1, 2, 3, and 4.

2. The compound according to claim 1, having Formulae (IIa)-(XIII):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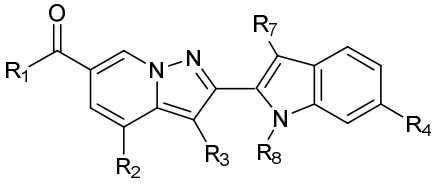
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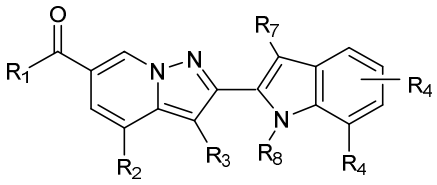
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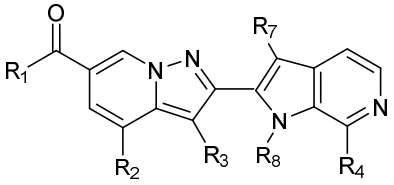
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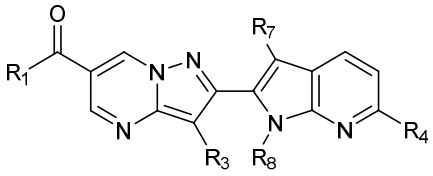
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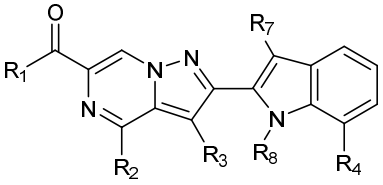
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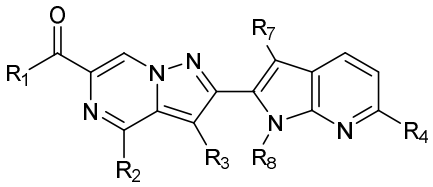
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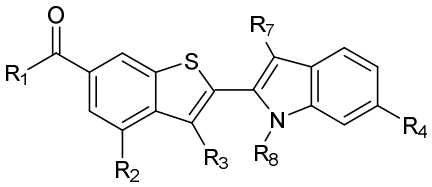
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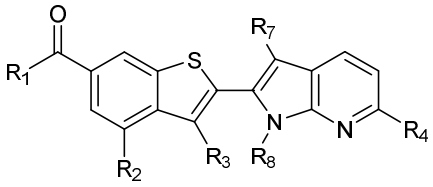
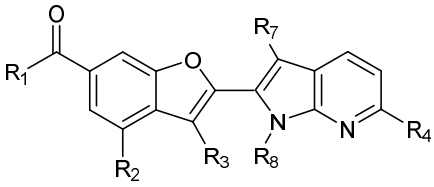

(X),

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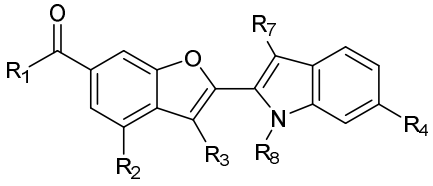
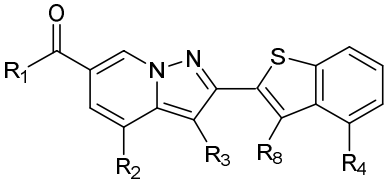
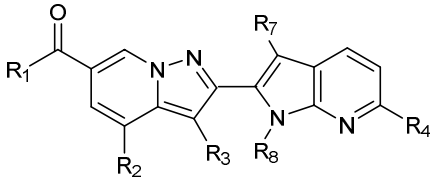
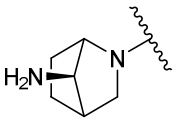
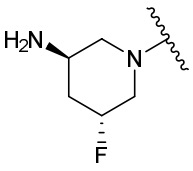
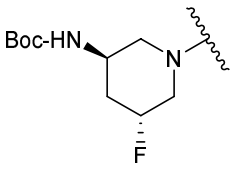
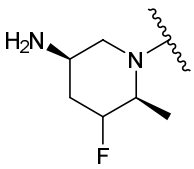
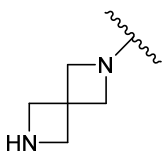
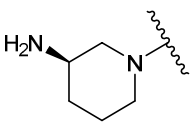
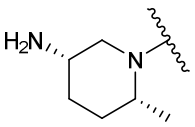

(XII), or

(XIII),
or a pharmaceutically acceptable salt thereof.

3. The compound according to claim 2, having Formula (IIa):



(IIa)

or a pharmaceutically acceptable salt thereof, wherein:

R_1 is independently selected from  ,  ,  ,  ,  ,  , and  ;

R_2 is independently selected from H, F, Cl, C_{1-3} alkyl optionally substituted with one or more substituents selected from F, Cl, and OH , and OC_{1-3} alkyl;

R_3 is independently selected from H, F, Cl, and C_{1-3} alkyl optionally substituted with one or more substituents selected from F, Cl, and OH;

R_4 is independently selected from H, F, Cl, -C(=O)R_b, C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –NH-C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –$(CH_2)_r$–aryl substituted with one or more R_5, -O-C_{1-6} alkyl substituted with one or more R_5, –$(CH_2)_r$–C_{3-12} cycloalkyl substituted with one or more R_5, and –$(CH_2)_r$–4–10 membered heterocyclyl comprising carbon atoms and 1–5 heteroatoms selected from N, NR_6, O, and S and substituted with one or more R_5;

R_5 is independently selected from H, F, Cl, =O, C_{1-4} alkyl optionally substituted with one or more R_e, –$(CH_2)_rOR_b$, –$(CH_2)_rS(O)_pR_c$, –$(CH_2)_rS(O)_pNR_aR_a$, –$(CH_2)_rNR_aS(O)_pR_c$, –$(CH_2)_rNR_aR_a$, –$(CH_2)_rNR_aC(=O)R_b$, –$(CH_2)_rNR_aC(=O)OR_b$, –$(CH_2)_rNR_aC(=O)NR_aR_a$, –$(CH_2)_rC(=O)R_b$, –$(CH_2)_rC(=O)OR_b$, –$(CH_2)_rC(=O)NR_aR_a$, –$(CH_2)_rOC(=O)R_b$, –$(CH_2)_rOC(=O)OR_b$, –$(CH_2)_rO(CH_2)_rC(=O)NR_aR_a$, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_6 is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, C(=O)R_b, -C(=O)NR_aR_a, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_7 is independently selected from H, F, and Cl;

R_8 is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, and C_{3-6} cycloalkyl;

R_a is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more R_e; or R_a and R_a together with the nitrogen atom to which they are both attached form a heterocyclic ring optionally substituted with one or more R_e;

R_b is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, $–(CH_2)_r–C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $–(CH_2)_r$ heterocyclyl optionally substituted with one or more R_e;

R_c is independently selected from C_{1-6} alkyl optionally substituted with one or more R_e, $–(CH_2)_r–C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $–(CH_2)_r–$ heterocyclyl optionally substituted with one or more R_e;

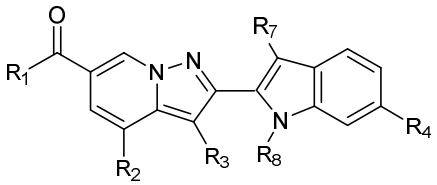
R_e is independently selected from F, Cl, Br, NH_2, $–NH\text{-}C_{1-4}$ alkyl, $–N(C_{1-4}$ alkyl$)_2$, =O, OH, $\text{-}OC_{1-6}$ alkyl, C_{1-6} alkyl optionally substituted with one or more R_f, $–(CH_2)_r–C_{3-6}$ cycloalkyl optionally substituted with one or more R_f, $–(CH_2)_r–$aryl optionally substituted with one or more R_f, and $–(CH_2)_r–$heterocyclyl optionally substituted with one or more R_f;

R_f is independently selected from F, Cl, OH, OC_{1-5} alkyl, C_{1-5} alkyl optionally substituted with OH, C_{3-6} cycloalkyl, and phenyl;

p, at each occurrence, is independently selected from zero, 1, and 2; and

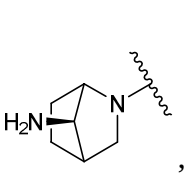
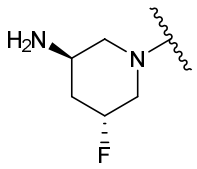
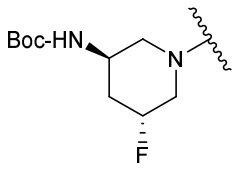
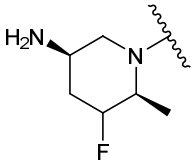
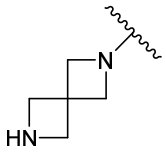
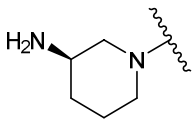
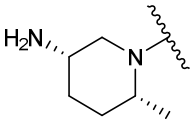
r, at each occurrence, is independently selected from zero, 1, 2, 3, and 4.

4. The compound according to claim 1, having Formula (IIIa):



(IIIa)

or a pharmaceutically acceptable salt thereof, wherein:

R_1 is independently selected from  ,  ,  ,  ,  ,  , and  ;

R_2 is independently selected from H, F, Cl, C_{1-3} alkyl optionally substituted with one or more substituents selected from F, Cl, and OH , and OC_{1-3} alkyl;

R_3 is independently selected from H, F, Cl, and C_{1-3} alkyl optionally substituted with one or more substituents selected from F, Cl, and OH;

R_4 is independently selected from H, F, Cl, -C(=O)R_b, C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –NH-C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –$(CH_2)_r$–aryl substituted with one or more R_5, -O-C_{1-6} alkyl substituted with one or more R_5, –$(CH_2)_r$–C_{3-12} cycloalkyl substituted with one or more R_5, and –$(CH_2)_r$–4–10 membered heterocyclyl comprising carbon atoms and 1–5 heteroatoms selected from N, NR_6, O, and S and substituted with one or more R_5;

R_5 is independently selected from H, F, Cl, =O, C_{1-4} alkyl optionally substituted with one or more R_e,–$(CH_2)_rOR_b$, –$(CH_2)_rS(O)_pR_c$, –$(CH_2)_rS(O)_pNR_aR_a$, –$(CH_2)_rNR_aS(O)_pR_c$, –$(CH_2)_rNR_aR_a$, –$(CH_2)_rNR_aC(=O)R_b$, –$(CH_2)_rNR_aC(=O)OR_b$, –$(CH_2)_rNR_aC(=O)NR_aR_a$, –$(CH_2)_rC(=O)R_b$, –$(CH_2)_rC(=O)OR_b$, –$(CH_2)_rC(=O)NR_aR_a$, –$(CH_2)_rOC(=O)R_b$, –$(CH_2)_rOC(=O)OR_b$, –$(CH_2)_rO(CH_2)_rC(=O)NR_aR_a$, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_6 is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, -C(=O)R_b, –C(=O)OR_b, -C(=O)NR_aR_a, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_7 is independently selected from H, F, and Cl;

R_8 is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, and C_{3-6} cycloalkyl;

R_a is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more R_e; or R_a and R_a together with the nitrogen atom to which they are both attached form a heterocyclic ring optionally substituted with one or more R_e;

R_b is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e,–$(CH_2)_r$–C_{3-10} carbocyclyl optionally substituted with one or more R_e, and –$(CH_2)_r$ heterocyclyl optionally substituted with one or more R_e;

R_c is independently selected from C_{1-6} alkyl optionally substituted with one or more R_e, –$(CH_2)_r$–C_{3-10} carbocyclyl optionally substituted with one or more R_e, and –$(CH_2)_r$–heterocyclyl optionally substituted with one or more R_e;

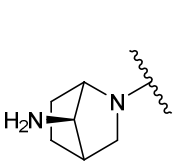
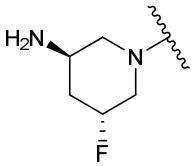
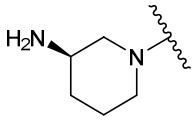
R_e is independently selected from F, Cl, Br, CN, NH_2, –NH-C_{1-4} alkyl, –N(C_{1-4} alkyl)$_2$, =O, OH, -OC_{1-6} alkyl, C_{1-6} alkyl optionally substituted with one or more R_f, –$(CH_2)_r$–C_{3-6} cycloalkyl optionally substituted with one or more R_f, –$(CH_2)_r$–aryl optionally substituted with one or more R_f, and –$(CH_2)_r$–heterocyclyl optionally substituted with one or more R_f;

R_f is independently selected from F, Cl, OH, OC_{1-5} alkyl, C_{1-5} alkyl optionally substituted with OH, C_{3-6} cycloalkyl, and phenyl;

p, at each occurrence, is independently selected from zero, 1, and 2; and

r, at each occurrence, is independently selected from zero, 1, 2, 3, and 4.

5. The compound according to claim 3 or 4, or a pharmaceutically acceptable salt thereof, wherein:

R_1 is independently selected from  ,  , and  ;

R_2 is independently selected from H, F, Cl, CH_3, and OCH_3;

R_3 is independently selected from H, F, Cl, CH_3, and CH_2OH;

R_4 is independently selected from H, F, Cl, C_{1-5} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl,–$(CH_2)_r$–aryl substituted with one or more R_5, -O-C_{1-6} alkyl substituted with one or more R_5, –$(CH_2)_r$–C_{3-12} cycloalkyl substituted with one or more R_5, and –$(CH_2)_r$–4–10 membered heterocyclyl comprising carbon atoms and 1–5 heteroatoms selected from N, NR_6, O, and S and substituted with one or more R_5;

R_5 is independently selected from H, F, Cl, =O, C_{1-4} alkyl optionally substituted with one or more R_e,–$(CH_2)_rOR_b$, –$(CH_2)_rS(O)_2R_c$, –$(CH_2)_rS(O)_pNR_aR_a$, –$(CH_2)_rNR_aS(O)_2R_c$, –$(CH_2)_rNR_aR_a$, –$(CH_2)_rNR_aC(=O)R_b$, –$(CH_2)_rNR_aC(=O)OR_b$, –$(CH_2)_rNR_aC(=O)NR_aR_a$, –$(CH_2)_rC(=O)R_b$, –$(CH_2)_rC(=O)OR_b$, –$(CH_2)_rC(=O)NR_aR_a$, –$(CH_2)_rOC(=O)R_b$, –$(CH_2)_rOC(=O)OR_b$, –$(CH_2)_rO(CH_2)_rC(=O)NR_aR_a$, C_{3-6} cycloalkyl optionally substituted with one or more

R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_6 is independently selected from H and C_{1-65} alkyl optionally substituted with one or more R_e;

R_7 is H;

R_8 is C_{1-3} alkyl substituted with one C_{3-6} cycloalkyl;

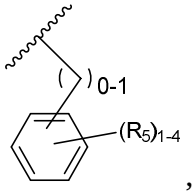
R_a is independently selected from H, and C_{1-4} alkyl;

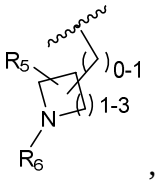
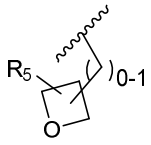
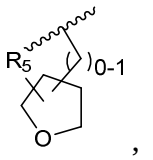
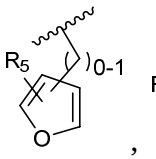
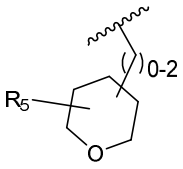
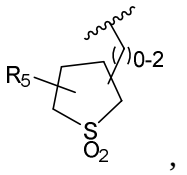
R_b is independently selected from H, C_{1-4} alkyl;

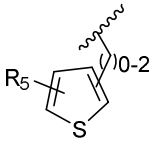
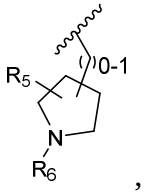
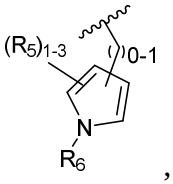
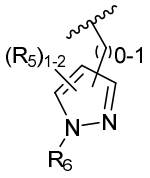
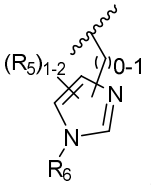
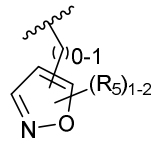
R_c is C_{1-4} alkyl; and

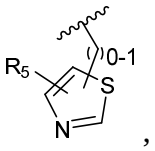
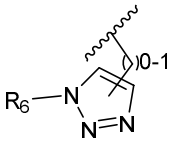
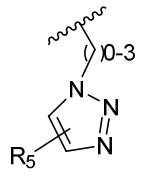
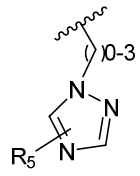
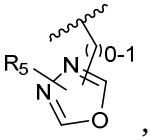
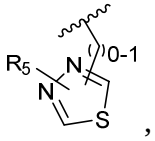
r, at each occurrence, is independently selected from zero, 1, and 2.

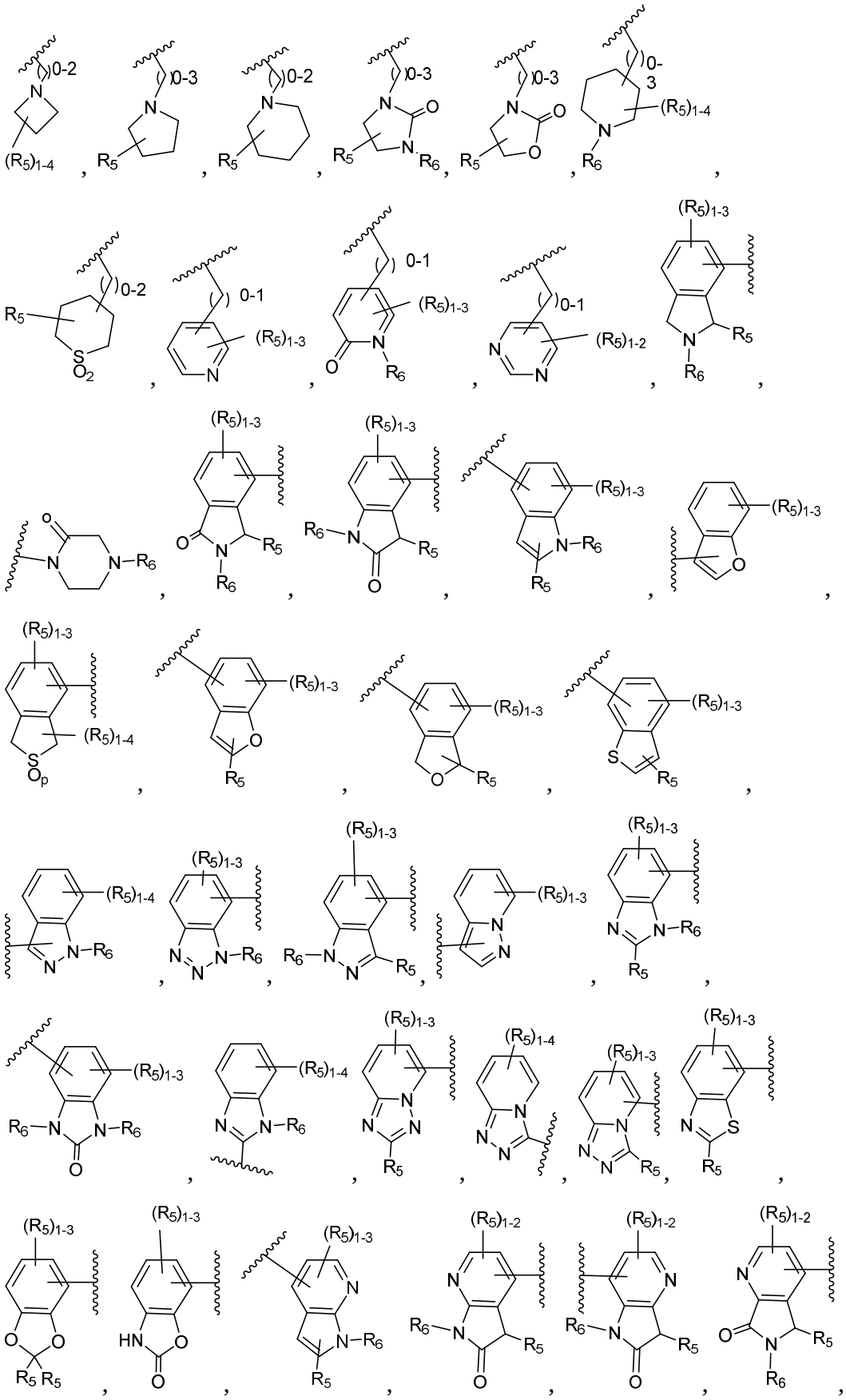
6. The compound according to claim 5, or a pharmaceutically acceptable salt thereof, wherein:

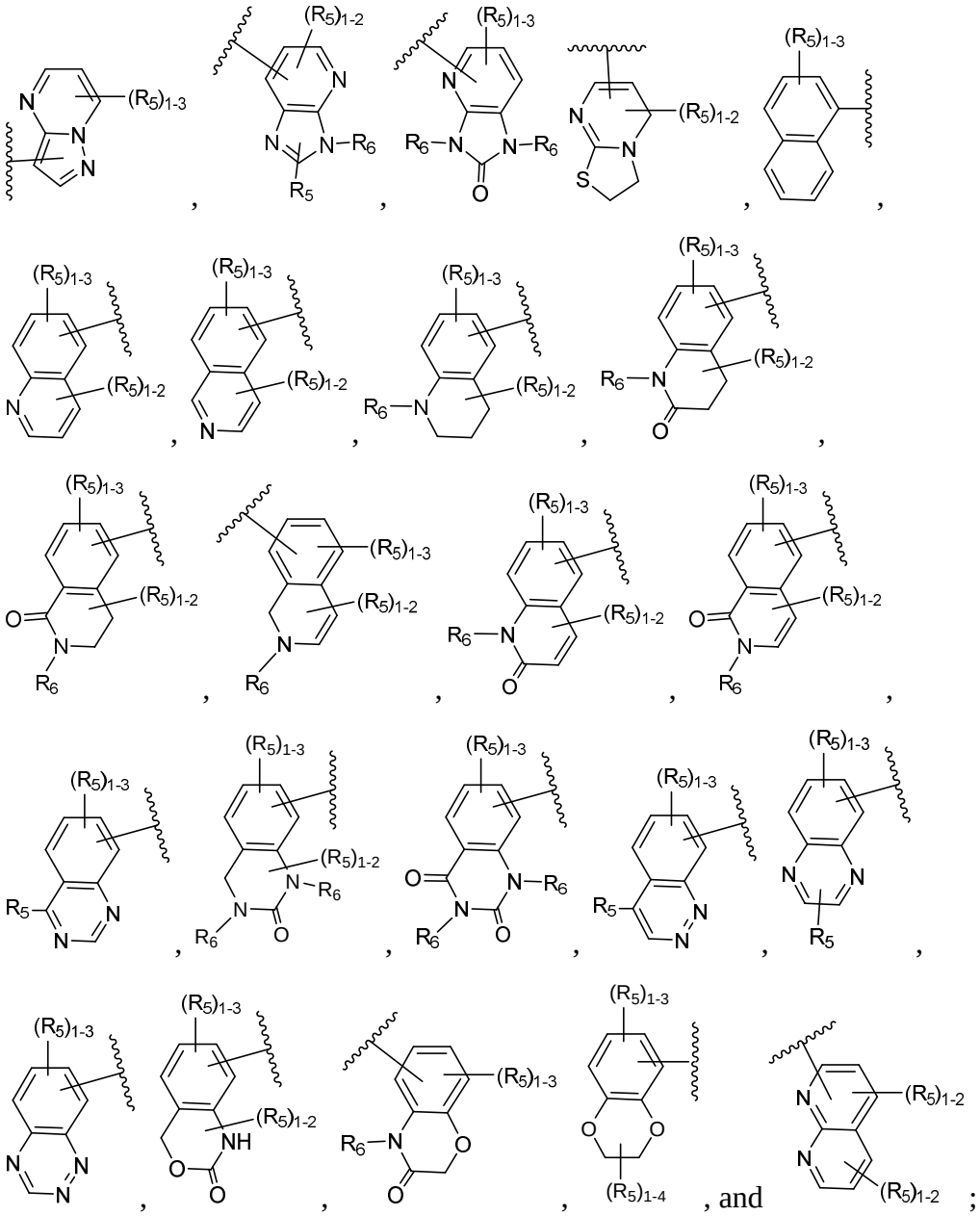
R_4 is independently selected from H, F, Cl, C_{1-5} alkyl optionally substituted with one or more substituents selected from F, Cl, and OH, C_{3-6} cycloalkyl,  ,

 ,  ,  ,  ,  ,  ,

 ,  ,  ,  ,  ,  ,

 ,  ,  ,  ,  ,  ,



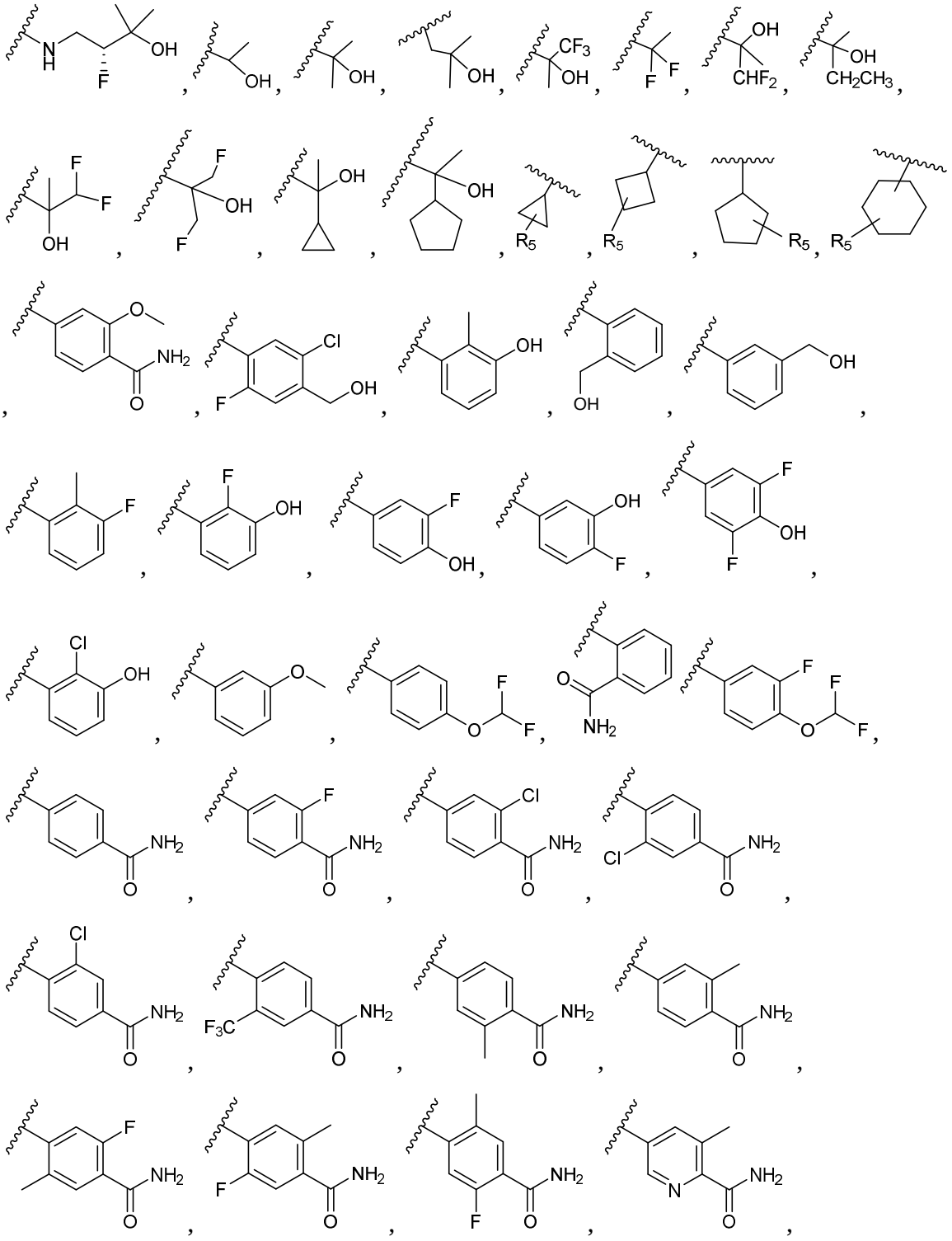


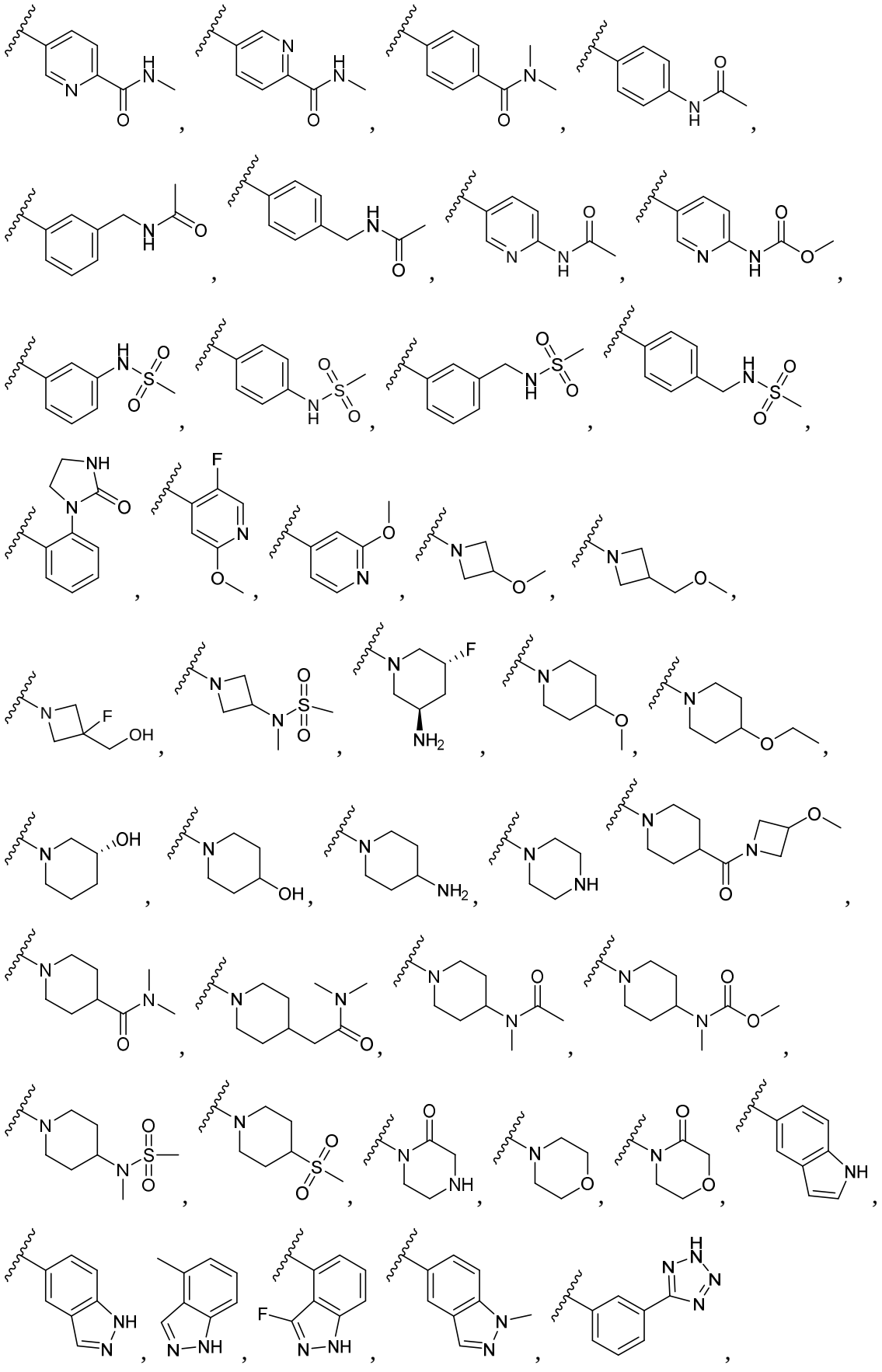
R_5 is independently selected from H, F, Cl, =O, C_{1-4} alkyl optionally substituted with one or more R_e,–$(CH_2)_rOR_b$, –$(CH_2)_rS(O)_pR_c$, –$(CH_2)_rS(O)_pNR_aR_a$, –$(CH_2)_rNR_aS(O)_pR_c$, –$(CH_2)_rNR_aR_a$, –$(CH_2)_rNR_aC(=O)R_b$, –$(CH_2)_rNR_aC(=O)OR_b$, –$(CH_2)_rNR_aC(=O)NR_aR_a$, –$(CH_2)_rC(=O)R_b$, –$(CH_2)_rC(=O)OR_b$, –$(CH_2)_rC(=O)NR_aR_a$, –$(CH_2)_rOC(=O)R_b$, –$(CH_2)_rOC(=O)OR_b$, –$(CH_2)_rO(CH_2)_rC(=O)NR_aR_a$, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e; and

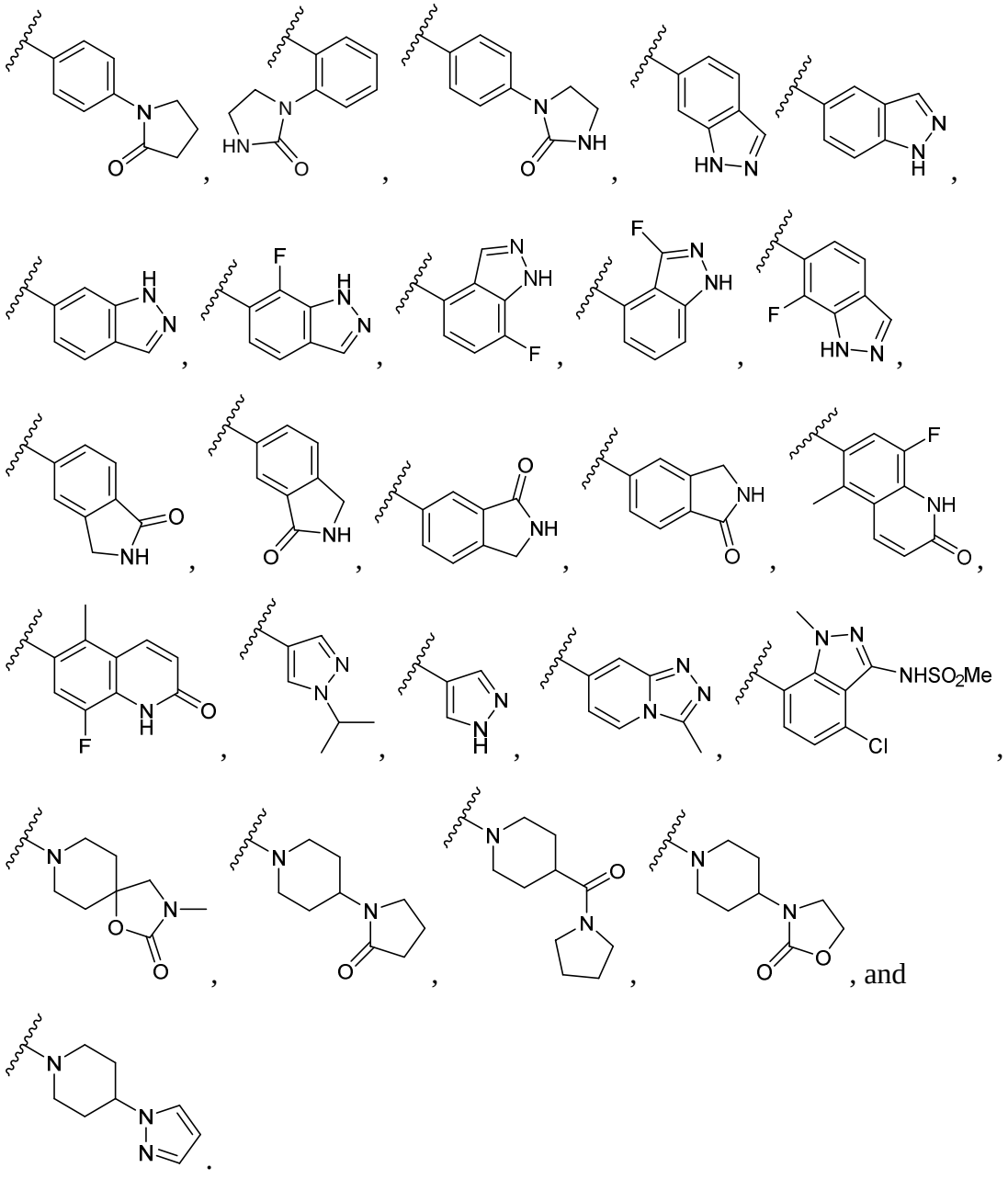
R_6 is independently selected from H and C_{1-5} alkyl.

7. The compound according to claim 6, or a pharmaceutically acceptable salt thereof, wherein:

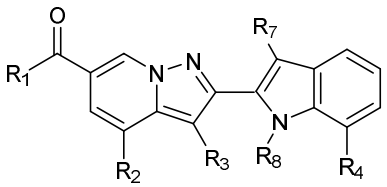
R_4 is independently selected from





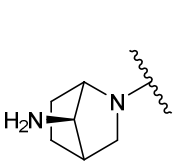
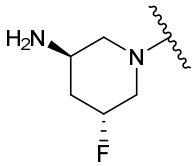
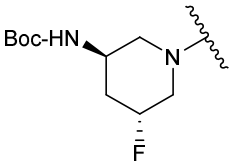
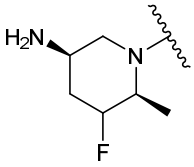
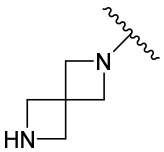
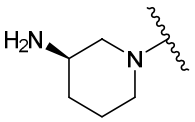
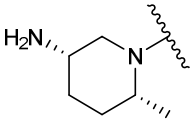


8. The compound according to claim 1, having Formula (IVa):



(IVa)

or a pharmaceutically acceptable salt thereof, wherein:

R_1 is independently selected from  ,  ,  ,  ,  ,  , and  ;

R_2 is independently selected from H, F, Cl, C_{1-3} alkyl optionally substituted with one or more substituents selected from F, Cl, and OH , and OC_{1-3} alkyl;

R_3 is independently selected from H, F, Cl, and C_{1-3} alkyl optionally substituted with one or more substituents selected from F, Cl, and OH;

R_4 is independently selected from H, F, Cl, -C(=O)R_b, C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –NH-C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –$(CH_2)_r$–aryl substituted with one or more R_5, -O-C_{1-6} alkyl substituted with one or more R_5, –$(CH_2)_r$–C_{3-12} cycloalkyl substituted with one or more R_5, and –$(CH_2)_r$–4–10 membered heterocyclyl comprising carbon atoms and 1–5 heteroatoms selected from N, NR_6, O, and S and substituted with one or more R_5;

R_5 is independently selected from H, F, Cl, =O, C_{1-4} alkyl optionally substituted with one or more R_e,–$(CH_2)_rOR_b$, –$(CH_2)_rS(O)_pR_c$, –$(CH_2)_rS(O)_pNR_aR_a$, –$(CH_2)_rNR_aS(O)_pR_c$, –$(CH_2)_rNR_aR_a$, –$(CH_2)_rNR_aC(=O)R_b$, –$(CH_2)_rNR_aC(=O)OR_b$, –$(CH_2)_rNR_aC(=O)NR_aR_a$, –$(CH_2)_rC(=O)R_b$, –$(CH_2)_rC(=O)OR_b$, –$(CH_2)_rC(=O)NR_aR_a$, –$(CH_2)_rOC(=O)R_b$, –$(CH_2)_rOC(=O)OR_b$, –$(CH_2)_rO(CH_2)_rC(=O)NR_aR_a$, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_6 is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, -$S(O)_pR_c$, -$S(O)_pNR_aR_a$, -C(=O)R_b, –C(=O)OR_b, -C(=O)NR_aR_a, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_7 is independently selected from H, F, and Cl;

R_8 is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, and C_{3-6} cycloalkyl;

R_a is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e,–$(CH_2)_r$–C_{3-10} carbocyclyl optionally substituted with one or more R_e, and –$(CH_2)_r$–heterocyclyl optionally substituted with one or more R_e; or R_a and R_a together with the nitrogen atom to which they are both attached form a heterocyclic ring optionally substituted with one or more R_e;

R_b is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e,–$(CH_2)_r$–C_{3-10} carbocyclyl optionally substituted with one or more R_e, and –$(CH_2)_r$ heterocyclyl optionally substituted with one or more R_e;

R_c is independently selected from C_{1-6} alkyl optionally substituted with one or more R_e,–$(CH_2)_r$–C_{3-10} carbocyclyl optionally substituted with one or more R_e, and –$(CH_2)_r$–heterocyclyl optionally substituted with one or more R_e;

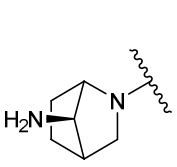
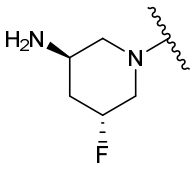
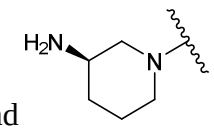
R_e is independently selected from F, Cl, Br, NH_2, –NH-C_{1-4} alkyl, –N(C_{1-4} alkyl)$_2$, =O, OH, -OC_{1-6} alkyl, C_{1-6} alkyl optionally substituted with one or more R_f, –$(CH_2)_r$–C_{3-6} cycloalkyl optionally substituted with one or more R_f, –$(CH_2)_r$–aryl optionally substituted with one or more R_f, and –$(CH_2)_r$–heterocyclyl optionally substituted with one or more R_f;

R_f is independently selected from F, Cl, OH, OC_{1-5} alkyl, C_{1-5} alkyl optionally substituted with OH, C_{2-5} alkenyl, C_{2-5} alkynyl, C_{3-6} cycloalkyl, and phenyl;

p, at each occurrence, is independently selected from zero, 1, and 2; and

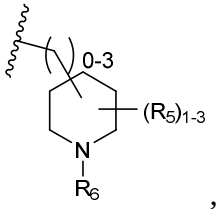
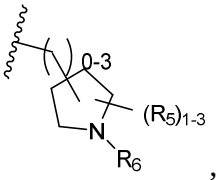
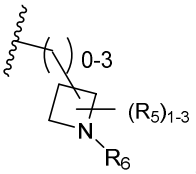
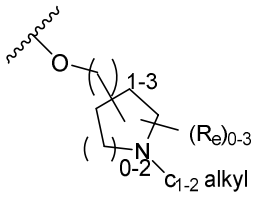
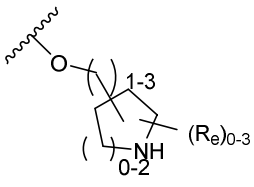
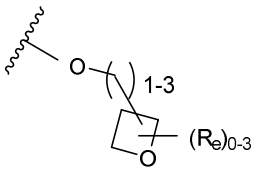
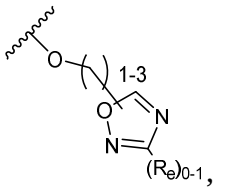
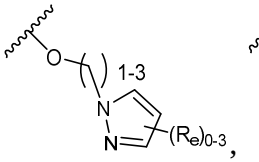
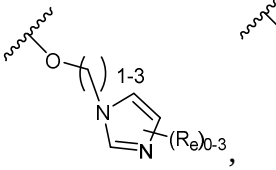
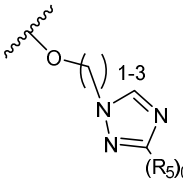
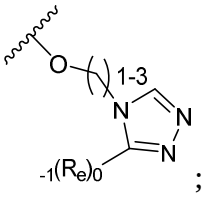
r, at each occurrence, is independently selected from zero, 1, 2, 3, and 4.

9. The compound according to claim 8, or a pharmaceutically acceptable salt thereof, wherein:

R_1 is independently selected from  ,  , and  ;

R_2 is independently selected from H, F, Cl, and OCH_3;

R_3 is independently selected from F, Cl, and CH_3;

R_4 is independently selected from H,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , and  ;

R_5 is independently selected from H, =O, $C_{1\text{-}4}$ alkyl, OH, and NH_2;

R_6 is independently selected from H, $C_{1\text{-}5}$ alkyl optionally substituted with one or more R_e, and -C(=O)R_b;

R_7 is H;

R_8 is $C_{1\text{-}2}$ alkyl optionally substituted with cyclopropyl;

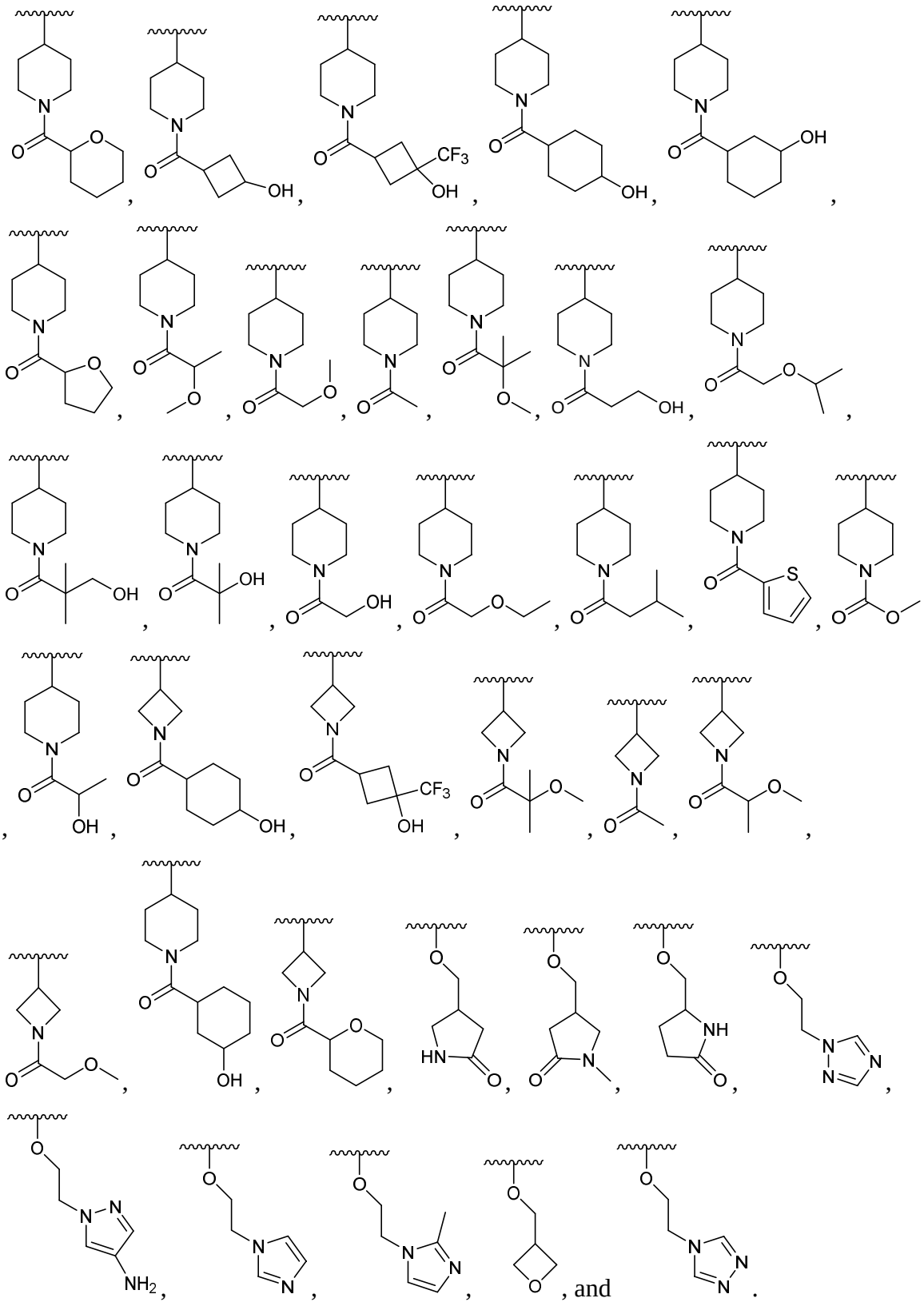
R_b is independently selected from H, $C_{1\text{-}6}$ alkyl optionally substituted with one or more R_e,–$(CH_2)_r$–$C_{3\text{-}10}$ carbocyclyl optionally substituted with one or more R_e, and –$(CH_2)_r$ heterocyclyl optionally substituted with one or more R_e;

R_e is independently selected from NH_2 and $C_{1\text{-}5}$ alkyl optionally substituted with one or more R_f; and

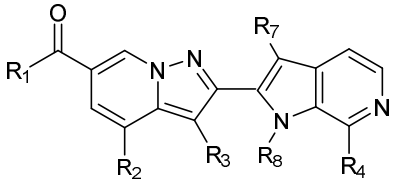
R_f is independently selected from F, Cl, OH, and $OC_{1\text{-}5}$ alkyl.

10. The compound according to claim 9, or a pharmaceutically acceptable salt thereof, wherein:

R_4 is independently selected from

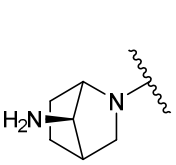
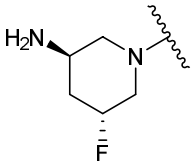
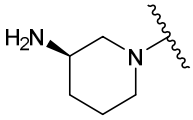


11. The compound according to claim 1, having Formula (Va):



(Va)

or a pharmaceutically acceptable salt thereof, wherein:

R_1 is independently selected from  ,  , and  ;

R_2 is independently selected from H, F, Cl, CH_3, and OCH_3;

R_3 is independently selected from H, F, Cl, CN, CH_3, and CH_2OH;

R_4 is independently selected from H, F, Cl, -C(=O)R_b, C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –NH-C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –$(CH_2)_r$–aryl substituted with one or more R_5, -O-C_{1-6} alkyl substituted with one or more R_5, –$(CH_2)_r$–C_{3-12} cycloalkyl substituted with one or more R_5, and –$(CH_2)_r$–4–10 membered heterocyclyl comprising carbon atoms and 1–5 heteroatoms selected from N, NR_6, O, and S and substituted with one or more R_5;

R_5 is independently selected from H, F, Cl, =O, C_{1-4} alkyl optionally substituted with one or more R_e,–$(CH_2)_rOR_b$, –$(CH_2)_rS(O)_pR_c$, –$(CH_2)_rS(O)_pNR_aR_a$, –$(CH_2)_rNR_aS(O)_pR_c$, –$(CH_2)_rNR_aR_a$, –$(CH_2)_rNR_aC(=O)R_b$, –$(CH_2)_rNR_aC(=O)OR_b$, –$(CH_2)_rNR_aC(=O)NR_aR_a$, –$(CH_2)_rC(=O)R_b$, –$(CH_2)_rC(=O)OR_b$, –$(CH_2)_rC(=O)NR_aR_a$, –$(CH_2)_rOC(=O)R_b$, –$(CH_2)_rOC(=O)OR_b$, –$(CH_2)_rO(CH_2)_rC(=O)NR_aR_a$, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_6 is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, -C(=O)R_b, –C(=O)OR_b, -C(=O)NR_aR_a, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_7 is independently selected from H, F, and Cl;

R_8 is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, and C_{3-6} cycloalkyl;

R_a is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e,–$(CH_2)_r$–C_{3-10} carbocyclyl optionally substituted with one or more R_e, and –$(CH_2)_r$–heterocyclyl optionally substituted with one or more R_e; or R_a and R_a together with the nitrogen atom to which they are both attached form a heterocyclic ring optionally substituted with one or more R_e;

R_b is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e,–$(CH_2)_r$–C_{3-10} carbocyclyl optionally substituted with one or more R_e, and –$(CH_2)_r$ heterocyclyl optionally substituted with one or more R_e;

R_c is independently selected from C_{1-6} alkyl optionally substituted with one or more R_e,–$(CH_2)_r$–C_{3-10} carbocyclyl optionally substituted with one or more R_e, and –$(CH_2)_r$–heterocyclyl optionally substituted with one or more R_e;

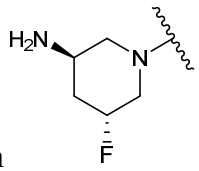
R_e is independently selected from F, Cl, Br, NH_2, –NH-C_{1-4} alkyl, –N(C_{1-4} alkyl)$_2$, =O, OH, -OC_{1-6} alkyl, –CO_2H, C_{1-6} alkyl optionally substituted with one or more R_f,–$(CH_2)_r$–C_{3-6} cycloalkyl optionally substituted with one or more R_f, –$(CH_2)_r$–aryl optionally substituted with one or more R_f, and –$(CH_2)_r$–heterocyclyl optionally substituted with one or more R_f;

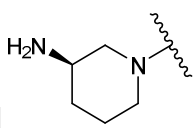
R_f is independently selected from F, Cl, Br, CN, OH, C_{1-5} alkyl optionally substituted with OH, C_{2-5} alkenyl, C_{2-5} alkynyl, C_{3-6} cycloalkyl, and phenyl;

p, at each occurrence, is independently selected from zero, 1, and 2; and

r, at each occurrence, is independently selected from zero, 1, 2, 3, and 4.

12. The compound according to claim 11, or a pharmaceutically acceptable salt thereof, wherein;

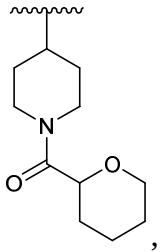
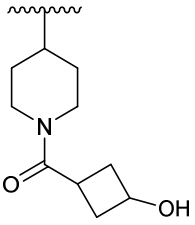
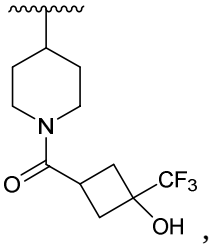
R_1 is independently selected from 

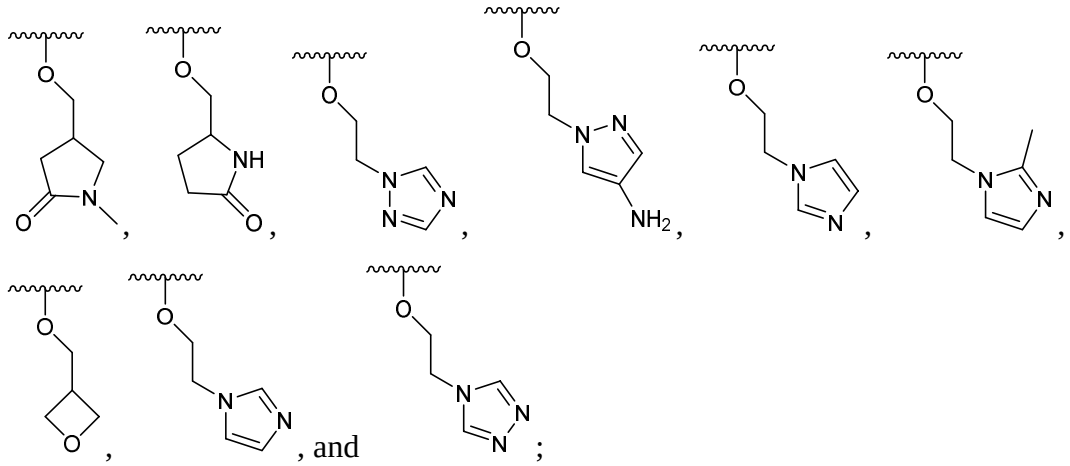
, and 

;

R_2 is CH_3;

R_3 is CH_3;

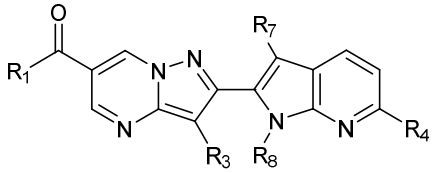
R_4 is independently selected from  ,  ,  ,



R_7 is H; and

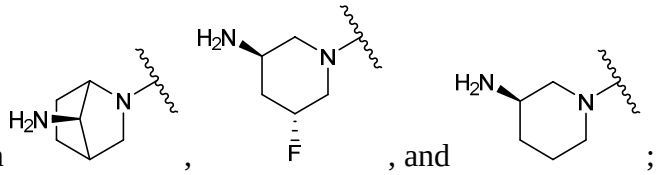
R_8 is C_{1-2} alkyl optionally substituted with cyclopropyl.

13. The compound according to claim 1, having Formula (VaI):



(VIa)

or a pharmaceutically acceptable salt thereof, wherein:

R_1 is independently selected from  ;

R_3 is independently selected from H, F, and CH_3;

R_4 is independently selected from H, F, Cl, -C(=O)R_b, C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –NH-C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –$(CH_2)_r$–aryl substituted with one or more R_5, -O-C_{1-6} alkyl substituted with one or more R_5, –$(CH_2)_r$–C_{3-12} cycloalkyl substituted with one or more R_5, and –$(CH_2)_r$–4–10 membered heterocyclyl comprising carbon atoms and 1–5 heteroatoms selected from N, NR_6, O, and S and substituted with one or more R_5;

R_5 is independently selected from H, F, Cl, Br, CN, =O, C_{1-4} alkyl optionally substituted with one or more R_e, C_{2-4} alkenyl optionally substituted with one or more R_e, C_{2-4}

alkynyl optionally substituted with one or more R_e, $–(CH_2)_rOR_b$, $–(CH_2)_rS(O)_pR_c$, $–(CH_2)_rS(O)_pNR_aR_a$, $–(CH_2)_rNR_aS(O)_pR_c$, $–(CH_2)_rNR_aR_a$, $–(CH_2)_rNR_aC(=O)R_b$, $–(CH_2)_rNR_aC(=O)OR_b$, $–(CH_2)_rNR_aC(=O)NR_aR_a$, $–(CH_2)_rC(=O)R_b$, $–(CH_2)_rC(=O)OR_b$, $–(CH_2)_rC(=O)NR_aR_a$, $–(CH_2)_rOC(=O)R_b$, $–(CH_2)_rOC(=O)OR_b$, $–(CH_2)_rO(CH_2)_rC(=O)NR_aR_a$, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_6 is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, $-C(=O)R_b$, $–C(=O)OR_b$, $-C(=O)NR_aR_a$, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_7 is independently selected from H, F, and Cl;

R_8 is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, and C_{3-6} cycloalkyl;

R_a is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more Re, C_{2-6} alkynyl optionally substituted with one or more R_e, $–(CH_2)_r–C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $–(CH_2)_r–$heterocyclyl optionally substituted with one or more R_e; or R_a and R_a together with the nitrogen atom to which they are both attached form a heterocyclic ring optionally substituted with one or more R_e;

R_b is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more R_e, C_{2-6} alkynyl optionally substituted with one or more R_e, $–(CH_2)_r–C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $–(CH_2)_r$ heterocyclyl optionally substituted with one or more R_e;

R_c is independently selected from C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more R_e, C_{2-6} alkynyl optionally substituted with one or more R_e, $–(CH_2)_r–C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $–(CH_2)_r–$heterocyclyl optionally substituted with one or more R_e;

R_e is independently selected from F, Cl, Br, CN, NH_2, $–NH-C_{1-4}$ alkyl, $–N(C_{1-4}$ alkyl$)_2$, =O, OH, $-OC_{1-6}$ alkyl, $–CO_2H$, C_{1-6} alkyl optionally substituted with one or more R_f,

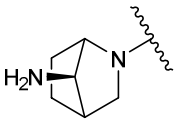
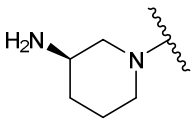
C_{2-6} alkenyl, C_{2-6} alkynyl, $–(CH_2)_r–C_{3-6}$ cycloalkyl optionally substituted with one or more R_f, $–(CH_2)_r–$aryl optionally substituted with one or more R_f, and $–(CH_2)_r–$heterocyclyl optionally substituted with one or more R_f;

R_f is independently selected from F, Cl, Br, CN, OH, C_{1-5} alkyl optionally substituted with OH, C_{2-5} alkenyl, C_{2-5} alkynyl, C_{3-6} cycloalkyl, and phenyl;

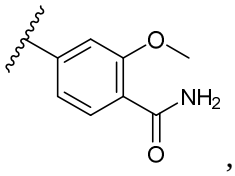
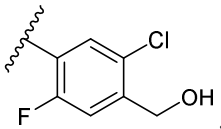
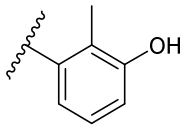
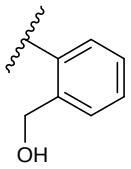
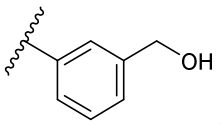
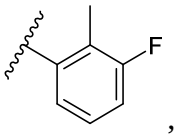
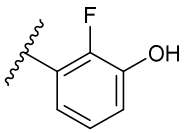
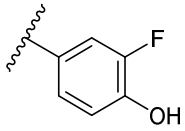
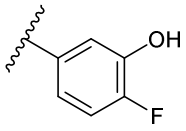
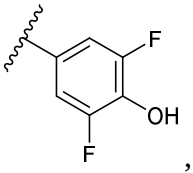
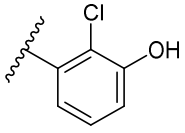
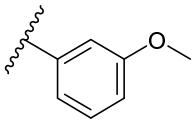
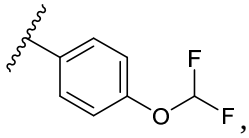
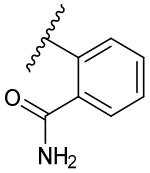
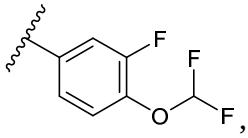
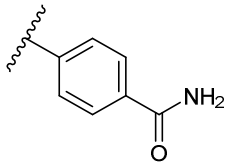
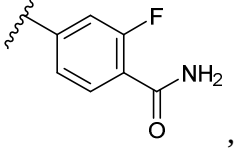
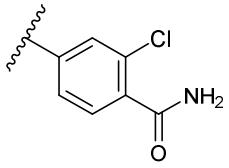
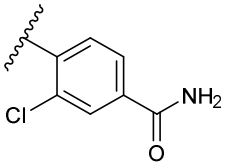
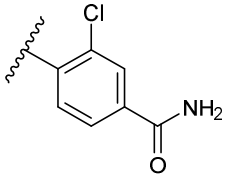
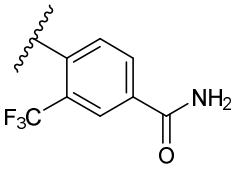
p, at each occurrence, is independently selected from zero, 1, and 2; and

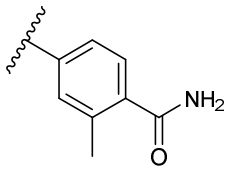
r, at each occurrence, is independently selected from zero, 1, 2, 3, and 4.

14. The compound according to claim 13, or a pharmaceutically acceptable salt thereof, wherein;

R_1 is independently selected from  and  ;

R_3 is CH_3;

R_4 is independently selected from F, Cl,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  .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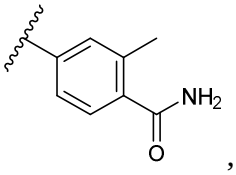
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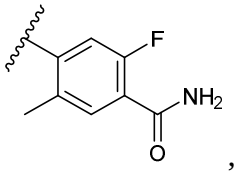
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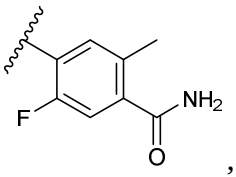
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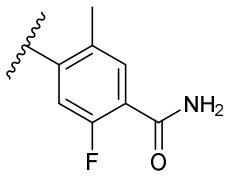
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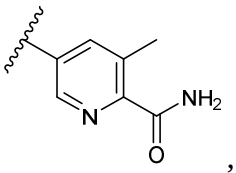
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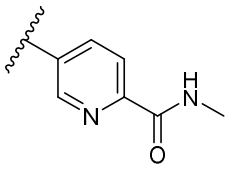
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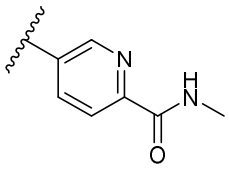
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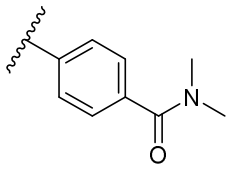
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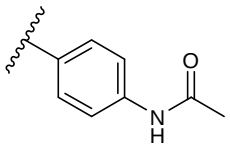
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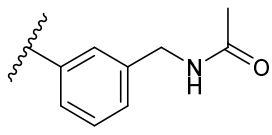
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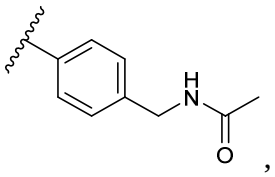
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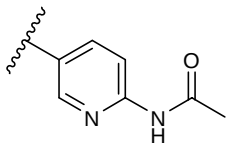
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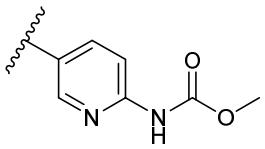
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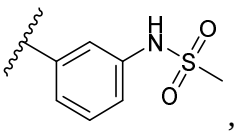
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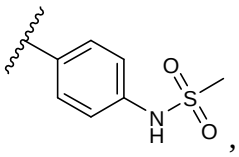
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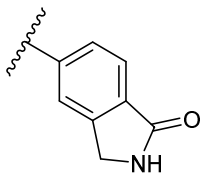
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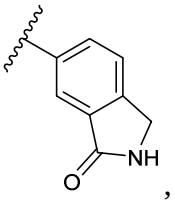
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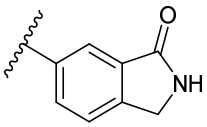
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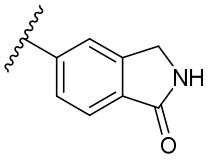
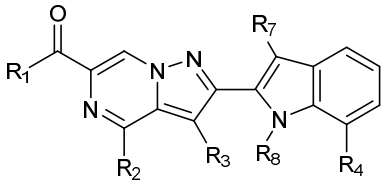

;

R_7 is H; and

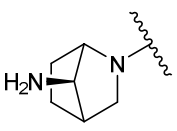
R_8 is $C_{1\text{-}2}$ alkyl optionally substituted with cyclopropyl.

15. The compound according to claim 1, having Formula (VII):



(VII)

or a pharmaceutically acceptable salt thereof, wherein:

R_1 is independently selected from

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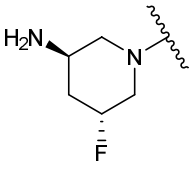
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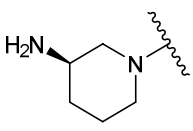

;

R_2 is independently selected from H, F, Cl, CH_3, and OCH_3;

R_3 is independently selected from H, F, and CH_3;

R_4 is independently selected from H, F, Cl, Br, -C(=O)R_b, C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –NH-C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –$(CH_2)_r$–aryl substituted with one or more R_5, -O-C_{1-6} alkyl substituted with one or more R_5, –$(CH_2)_r$–C_{3-12} cycloalkyl substituted with one or more R_5, and –$(CH_2)_r$–4–10 membered heterocyclyl comprising carbon atoms and 1–5 heteroatoms selected from N, NR_6, O, and S and substituted with one or more R_5;

R_5 is independently selected from H, F, Cl, Br, CN, =O, C_{1-4} alkyl optionally substituted with one or more R_e, C_{2-4} alkenyl optionally substituted with one or more R_e, C_{2-4} alkynyl optionally substituted with one or more R_e, –$(CH_2)_r$$OR_b$, –$(CH_2)_r$$S(O)_pR_c$, –$(CH_2)_r$$S(O)_pNR_aR_a$, –$(CH_2)_r$$NR_aS(O)_pR_c$, –$(CH_2)_r$$NR_aR_a$, –$(CH_2)_r$$NR_aC(=O)R_b$, –$(CH_2)_r$$NR_aC(=O)OR_b$, –$(CH_2)_r$$NR_aC(=O)NR_aR_a$, –$(CH_2)_r$$C(=O)R_b$, –$(CH_2)_r$$C(=O)OR_b$, –$(CH_2)_r$$C(=O)NR_aR_a$, –$(CH_2)_r$$OC(=O)R_b$, –$(CH_2)_r$$OC(=O)OR_b$, –$(CH_2)_r$$O(CH_2)_rC(=O)NR_aR_a$, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_6 is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, -$S(O)_pR_c$, -$S(O)_pNR_aR_a$, -C(=O)R_b, –C(=O)OR_b, -C(=O)NR_aR_a, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_7 is independently selected from H, F, and Cl;

R_8 is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, and C_{3-6} cycloalkyl;

R_a is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more Re, C_{2-6} alkynyl optionally substituted with one or more R_e, –$(CH_2)_r$–C_{3-10} carbocyclyl optionally substituted with one or more R_e, and –$(CH_2)_r$–heterocyclyl optionally substituted with one or more R_e; or R_a and R_a together with the nitrogen atom to which they are both attached form a heterocyclic ring optionally substituted with one or more R_e;

R_b is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more R_e, C_{2-6} alkynyl optionally substituted with one or more R_e, $–(CH_2)_r–C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $–(CH_2)_r$ heterocyclyl optionally substituted with one or more R_e;

R_c is independently selected from C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more R_e, C_{2-6} alkynyl optionally substituted with one or more R_e, $–(CH_2)_r–C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $–(CH_2)_r–$heterocyclyl optionally substituted with one or more R_e;

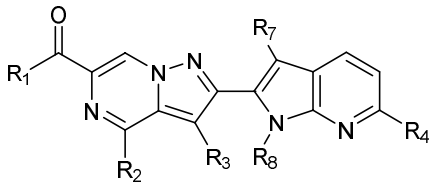
R_e is independently selected from F, Cl, Br, CN, NH_2, $–NH\text{-}C_{1-4}$ alkyl, $–N(C_{1-4}$ alkyl$)_2$, =O, OH, $\text{-}OC_{1-6}$ alkyl, $–CO_2H$, C_{1-6} alkyl optionally substituted with one or more R_f, C_{2-6} alkenyl, C_{2-6} alkynyl, $–(CH_2)_r–C_{3-6}$ cycloalkyl optionally substituted with one or more R_f, $–(CH_2)_r–$aryl optionally substituted with one or more R_f, and $–(CH_2)_r–$heterocyclyl optionally substituted with one or more R_f;

R_f is independently selected from F, Cl, Br, CN, OH, C_{1-5} alkyl optionally substituted with OH, C_{2-5} alkenyl, C_{2-5} alkynyl, C_{3-6} cycloalkyl, and phenyl;

p, at each occurrence, is independently selected from zero, 1, and 2; and

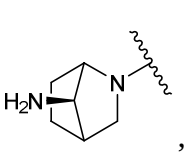
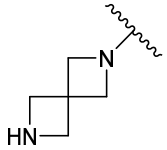
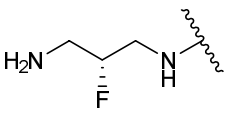
r, at each occurrence, is independently selected from zero, 1, 2, 3, and 4.

16. The compound according to claim 1, having Formula (VIII):



(VIII)

or a pharmaceutically acceptable salt thereof, wherein:

R_1 is independently selected from  ,  , and  ;

R_2 is independently selected from H, F, and OCH_3;

R_3 is independently selected from H, F, and CH_3;

R_4 is independently selected from H, F, Cl, Br, -C(=O)R_b, C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –NH-C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –$(CH_2)_r$–aryl substituted with one or more R_5, -O-C_{1-6} alkyl substituted with one or more R_5, –$(CH_2)_r$–C_{3-12} cycloalkyl substituted with one or more R_5, and –$(CH_2)_r$–4–10 membered heterocyclyl comprising carbon atoms and 1–5 heteroatoms selected from N, NR_6, O, and S and substituted with one or more R_5;

R_5 is independently selected from H, F, Cl, Br, CN, =O, C_{1-4} alkyl optionally substituted with one or more R_e, C_{2-4} alkenyl optionally substituted with one or more R_e, C_{2-4} alkynyl optionally substituted with one or more R_e, –$(CH_2)_r$$OR_b$, –$(CH_2)_r$$S(O)_pR_c$, –$(CH_2)_r$$S(O)_pNR_aR_a$, –$(CH_2)_r$$NR_aS(O)_pR_c$, –$(CH_2)_r$$NR_aR_a$, –$(CH_2)_r$$NR_aC(=O)R_b$, –$(CH_2)_r$$NR_aC(=O)OR_b$, –$(CH_2)_r$$NR_aC(=O)NR_aR_a$, –$(CH_2)_r$$C(=O)R_b$, –$(CH_2)_r$$C(=O)OR_b$, –$(CH_2)_r$$C(=O)NR_aR_a$, –$(CH_2)_r$$OC(=O)R_b$, –$(CH_2)_r$$OC(=O)OR_b$, –$(CH_2)_r$$O(CH_2)_rC(=O)NR_aR_a$, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_6 is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, -C(=O)R_b, –C(=O)OR_b, -C(=O)NR_aR_a, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_7 is independently selected from H, F, and Cl;

R_8 is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, and C_{3-6} cycloalkyl;

R_a is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more Re, C_{2-6} alkynyl optionally substituted with one or more R_e, –$(CH_2)_r$–C_{3-10} carbocyclyl optionally substituted with one or more R_e, and –$(CH_2)_r$–heterocyclyl optionally substituted with one or more R_e; or R_a and R_a together with the nitrogen atom to which they are both attached form a heterocyclic ring optionally substituted with one or more R_e;

R_b is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more R_e, C_{2-6} alkynyl optionally

substituted with one or more R_e, $–(CH_2)_r–C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $–(CH_2)_r$ heterocyclyl optionally substituted with one or more R_e;

R_c is independently selected from C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more R_e, C_{2-6} alkynyl optionally substituted with one or more R_e, $–(CH_2)_r–C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $–(CH_2)_r–$heterocyclyl optionally substituted with one or more R_e;

R_d is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more R_e;

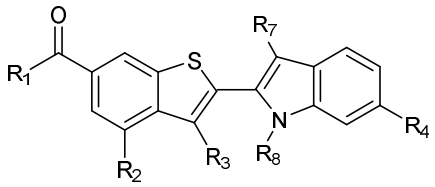
R_e is independently selected from F, Cl, Br, CN, NH_2, $–NH\text{-}C_{1-4}$ alkyl, $–N(C_{1-4}$ alkyl$)_2$, =O, OH, $\text{-}OC_{1-6}$ alkyl, $–CO_2H$, C_{1-6} alkyl optionally substituted with one or more R_f, C_{2-6} alkenyl, C_{2-6} alkynyl, $–(CH_2)_r–C_{3-6}$ cycloalkyl optionally substituted with one or more R_f, $–(CH_2)_r–$aryl optionally substituted with one or more R_f, and $–(CH_2)_r–$heterocyclyl optionally substituted with one or more R_f;

R_f is independently selected from F, Cl, Br, CN, OH, C_{1-5} alkyl optionally substituted with OH, C_{2-5} alkenyl, C_{2-5} alkynyl, C_{3-6} cycloalkyl, and phenyl;

p, at each occurrence, is independently selected from zero, 1, and 2; and

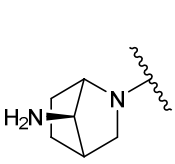
r, at each occurrence, is independently selected from zero, 1, 2, 3, and 4.

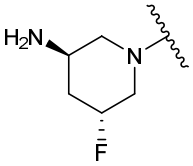
17. The compound according to claim 1, having Formula (IX):

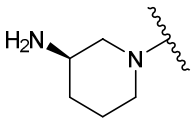


(IX)

or a pharmaceutically acceptable salt thereof, wherein:

R_1 is independently selected from 

, 

, and 

;

R_2 is independently selected from H, F, CH_3, CH_2OH, CH_2CH_2OH, and OCH_3;

R_3 is independently selected from H, F, Cl, CH_3, CH_2OH, CH_2CH_2OH, CH_2NH_3, $CH_2CH_2NH_2$, and $CH_2CH_2N_3$;

R_4 is independently selected from H, F, Cl, Br, -$C(=O)R_b$, C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –NH-C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, $–(CH_2)_r–$aryl substituted with one or more R_5, -O-C_{1-6} alkyl substituted with one or more R_5, $–(CH_2)_r–C_{3-12}$ cycloalkyl substituted with one or more R_5, and $–(CH_2)_r–$4–10 membered heterocyclyl comprising carbon atoms and 1–5 heteroatoms selected from N, NR_6, O, and S and substituted with one or more R_5;

R_5 is independently selected from H, F, Cl, Br, CN, =O, C_{1-4} alkyl optionally substituted with one or more R_e, C_{2-4} alkenyl optionally substituted with one or more R_e, C_{2-4} alkynyl optionally substituted with one or more R_e, $–(CH_2)_rOR_b$, $–(CH_2)_rS(O)_pR_c$, $–(CH_2)_rS(O)_pNR_aR_a$, $–(CH_2)_rNR_aS(O)_pR_c$, $–(CH_2)_rNR_aR_a$, $–(CH_2)_rNR_aC(=O)R_b$, $–(CH_2)_rNR_aC(=O)OR_b$, $–(CH_2)_rNR_aC(=O)NR_aR_a$, $–(CH_2)_rC(=O)R_b$, $–(CH_2)_rC(=O)OR_b$, $–(CH_2)_rC(=O)NR_aR_a$, $–(CH_2)_rOC(=O)R_b$, $–(CH_2)_rOC(=O)OR_b$, $–(CH_2)_rO(CH_2)_rC(=O)NR_aR_a$, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_6 is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, -$S(O)_pR_c$, -$S(O)_pNR_aR_a$, -$C(=O)R_b$, $–C(=O)OR_b$, -$C(=O)NR_aR_a$, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_7 is independently selected from H, F, and Cl;

R_8 is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, and C_{3-6} cycloalkyl;

R_a is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more Re, C_{2-6} alkynyl optionally substituted with one or more R_e, $–(CH_2)_r–C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $–(CH_2)_r–$heterocyclyl optionally substituted with one or more R_e; or R_a and R_a together with the nitrogen atom to which they are both attached form a heterocyclic ring optionally substituted with one or more R_e;

R_b is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more R_e, C_{2-6} alkynyl optionally substituted with one or more R_e, $–(CH_2)_r–C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $–(CH_2)_r$ heterocyclyl optionally substituted with one or more R_e;

R_c is independently selected from C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more R_e, C_{2-6} alkynyl optionally substituted with one or more R_e, $–(CH_2)_r–C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $–(CH_2)_r–$heterocyclyl optionally substituted with one or more R_e;

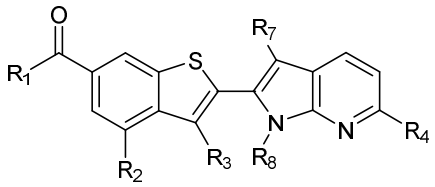
R_e is independently selected from F, Cl, Br, CN, NH_2, $–NH\text{-}C_{1-4}$ alkyl, $–N(C_{1-4}$ alkyl$)_2$, =O, OH, $\text{-}OC_{1-6}$ alkyl, $–CO_2H$, C_{1-6} alkyl optionally substituted with one or more R_f, C_{2-6} alkenyl, C_{2-6} alkynyl, $–(CH_2)_r–C_{3-6}$ cycloalkyl optionally substituted with one or more R_f, $–(CH_2)_r–$aryl optionally substituted with one or more R_f, and $–(CH_2)_r–$heterocyclyl optionally substituted with one or more R_f;

R_f is independently selected from F, Cl, Br, CN, OH, C_{1-5} alkyl optionally substituted with OH, C_{2-5} alkenyl, C_{2-5} alkynyl, C_{3-6} cycloalkyl, and phenyl;

p, at each occurrence, is independently selected from zero, 1, and 2; and

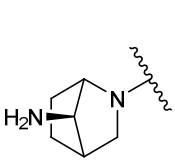
r, at each occurrence, is independently selected from zero, 1, 2, 3, and 4.

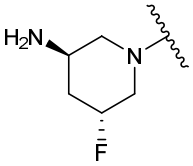
18. The compound according to claim 1, having Formula (X):

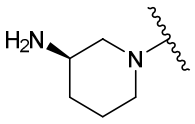


(X)

or a pharmaceutically acceptable salt thereof, wherein:

R_1 is independently selected from 

, 

, and 

;

R_2 is independently selected from H, FCH_3,CH_2OH, CH_2CH_2OH, and OCH_3;

R_3 is independently selected from H, F, CH_3, CH_2OH, CH_2CH_2OH, CH_2NH_3, $CH_2CH_2NH_2$, and $CH_2CH_2N_3$;

R_4 is independently selected from H, F, Cl, Br, -C(=O)R_b, C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –NH-C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –$(CH_2)_r$–aryl substituted with one or more R_5, -O-C_{1-6} alkyl substituted with one or more R_5, –$(CH_2)_r$–C_{3-12} cycloalkyl substituted with one or more R_5, and –$(CH_2)_r$–4–10 membered heterocyclyl comprising carbon atoms and 1–5 heteroatoms selected from N, NR_6, O, and S and substituted with one or more R_5;

R_5 is independently selected from H, F, Cl, Br, CN, =O, C_{1-4} alkyl optionally substituted with one or more R_e, C_{2-4} alkenyl optionally substituted with one or more R_e, C_{2-4} alkynyl optionally substituted with one or more R_e, –$(CH_2)_rOR_b$, –$(CH_2)_rS(O)_pR_c$, –$(CH_2)_rS(O)_pNR_aR_a$, –$(CH_2)_rNR_aS(O)_pR_c$, –$(CH_2)_rNR_aR_a$, –$(CH_2)_rNR_aC(=O)R_b$, –$(CH_2)_rNR_aC(=O)OR_b$, –$(CH_2)_rNR_aC(=O)NR_aR_a$, –$(CH_2)_rC(=O)R_b$, –$(CH_2)_rC(=O)OR_b$, –$(CH_2)_rC(=O)NR_aR_a$, –$(CH_2)_rOC(=O)R_b$, –$(CH_2)_rOC(=O)OR_b$, –$(CH_2)_rO(CH_2)_rC(=O)NR_aR_a$, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_6 is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, -$S(O)_pR_c$, -$S(O)_pNR_aR_a$, -C(=O)R_b, –C(=O)OR_b, -C(=O)NR_aR_a, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_7 is independently selected from H, F, and Cl;

R_8 is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, and C_{3-6} cycloalkyl;

R_a is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more Re, C_{2-6} alkynyl optionally substituted with one or more R_e, –$(CH_2)_r$–C_{3-10} carbocyclyl optionally substituted with one or more R_e, and –$(CH_2)_r$–heterocyclyl optionally substituted with one or more R_e; or R_a and R_a together with the nitrogen atom to which they are both attached form a heterocyclic ring optionally substituted with one or more R_e;

R_b is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more R_e, C_{2-6} alkynyl optionally substituted with one or more R_e, $–(CH_2)_r–C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $–(CH_2)_r$ heterocyclyl optionally substituted with one or more R_e;

R_c is independently selected from C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more R_e, C_{2-6} alkynyl optionally substituted with one or more R_e, $–(CH_2)_r–C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $–(CH_2)_r–$heterocyclyl optionally substituted with one or more R_e;

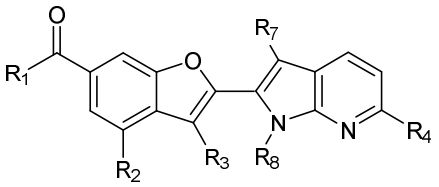
R_e is independently selected from F, Cl, Br, CN, NH_2, $–NH-C_{1-4}$ alkyl, $–N(C_{1-4}$ alkyl$)_2$, =O, OH, $-OC_{1-6}$ alkyl, $–CO_2H$, C_{1-6} alkyl optionally substituted with one or more R_f, C_{2-6} alkenyl, C_{2-6} alkynyl, $–(CH_2)_r–C_{3-6}$ cycloalkyl optionally substituted with one or more R_f, $–(CH_2)_r–$aryl optionally substituted with one or more R_f, and $–(CH_2)_r–$heterocyclyl optionally substituted with one or more R_f;

R_f is independently selected from F, Cl, Br, CN, OH, C_{1-5} alkyl optionally substituted with OH, C_{2-5} alkenyl, C_{2-5} alkynyl, C_{3-6} cycloalkyl, and phenyl;

p, at each occurrence, is independently selected from zero, 1, and 2; and

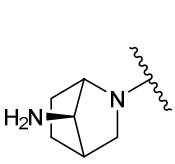
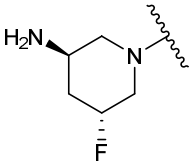
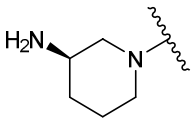
r, at each occurrence, is independently selected from zero, 1, 2, 3, and 4.

19. The compound according to claim 1, having Formula (XI):



(XI)

or a pharmaceutically acceptable salt thereof, wherein:

R_1 is independently selected from  ,  , and  ;

R_2 is independently selected from H, F, CH_3, CH_2OH, CH_2CH_2OH, and OCH_3;

R_3 is independently selected from H, F, CH_3, CH_2OH, CH_2CH_2OH, CH_2NH_3, $CH_2CH_2NH_2$, and $CH_2CH_2N_3$;

R_4 is independently selected from H, F, Cl, Br, -$C(=O)R_b$, C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –NH-C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –$(CH_2)_r$–aryl substituted with one or more R_5, -O-C_{1-6} alkyl substituted with one or more R_5, –$(CH_2)_r$–C_{3-12} cycloalkyl substituted with one or more R_5, and –$(CH_2)_r$–4–10 membered heterocyclyl comprising carbon atoms and 1–5 heteroatoms selected from N, NR_6, O, and S and substituted with one or more R_5;

R_5 is independently selected from H, F, Cl, Br, CN, =O, C_{1-4} alkyl optionally substituted with one or more R_e, C_{2-4} alkenyl optionally substituted with one or more R_e, C_{2-4} alkynyl optionally substituted with one or more R_e, –$(CH_2)_rOR_b$, –$(CH_2)_rS(O)_pR_c$, –$(CH_2)_rS(O)_pNR_aR_a$, –$(CH_2)_rNR_aS(O)_pR_c$, –$(CH_2)_rNR_aR_a$, –$(CH_2)_rNR_aC(=O)R_b$, –$(CH_2)_rNR_aC(=O)OR_b$, –$(CH_2)_rNR_aC(=O)NR_aR_a$, –$(CH_2)_rC(=O)R_b$, –$(CH_2)_rC(=O)OR_b$, –$(CH_2)_rC(=O)NR_aR_a$, –$(CH_2)_rOC(=O)R_b$, –$(CH_2)_rOC(=O)OR_b$, –$(CH_2)_rO(CH_2)_rC(=O)NR_aR_a$, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_6 is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, -$S(O)_pR_c$, -$S(O)_pNR_aR_a$, -$C(=O)R_b$, –$C(=O)OR_b$, -$C(=O)NR_aR_a$, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_7 is independently selected from H, F, and Cl;

R_8 is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, and C_{3-6} cycloalkyl;

R_a is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more Re, C_{2-6} alkynyl optionally substituted with one or more R_e, –$(CH_2)_r$–C_{3-10} carbocyclyl optionally substituted with one or more R_e, and –$(CH_2)_r$–heterocyclyl optionally substituted with one or more R_e; or R_a and R_a together with the nitrogen atom to which they are both attached form a heterocyclic ring optionally substituted with one or more R_e;

R_b is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more R_e, C_{2-6} alkynyl optionally substituted with one or more R_e, $–(CH_2)_r–C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $–(CH_2)_r$ heterocyclyl optionally substituted with one or more R_e;

R_c is independently selected from C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more R_e, C_{2-6} alkynyl optionally substituted with one or more R_e, $–(CH_2)_r–C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $–(CH_2)_r–$heterocyclyl optionally substituted with one or more R_e;

R_d is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more R_e;

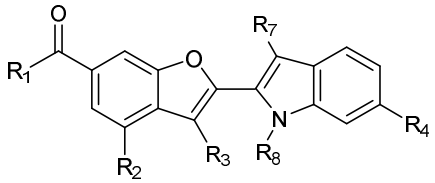
R_e is independently selected from F, Cl, Br, CN, NH_2, $–NH-C_{1-4}$ alkyl, $–N(C_{1-4}$ alkyl$)_2$, =O, OH, $-OC_{1-6}$ alkyl, $–CO_2H$, C_{1-6} alkyl optionally substituted with one or more R_f, C_{2-6} alkenyl, C_{2-6} alkynyl, $–(CH_2)_r–C_{3-6}$ cycloalkyl optionally substituted with one or more R_f, $–(CH_2)_r–$aryl optionally substituted with one or more R_f, and $–(CH_2)_r–$heterocyclyl optionally substituted with one or more R_f;

R_f is independently selected from F, Cl, Br, CN, OH, C_{1-5} alkyl optionally substituted with OH, C_{2-5} alkenyl, C_{2-5} alkynyl, C_{3-6} cycloalkyl, and phenyl;

p, at each occurrence, is independently selected from zero, 1, and 2; and

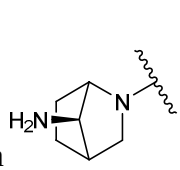
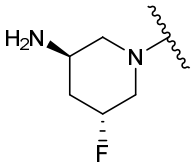
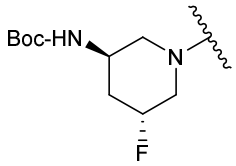
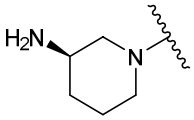
r, at each occurrence, is independently selected from zero, 1, 2, 3, and 4.

20. The compound according to claim 1, having Formula (XII):



(XII)

or a pharmaceutically acceptable salt thereof, wherein:

R_1 is independently selected from  ,  ,  , and  ;

R_2 is independently selected from H, F, CH_3, CH_2OH, CH_2CH_2OH and OCH_3;

R_3 is independently selected from H, F, and CH_3, CH_2OH, CH_2CH_2OH, CH_2NH_3, $CH_2CH_2NH_2$, and $CH_2CH_2N_3$;

R_4 is independently selected from H, F, Cl, Br, -C(=O)R_b, C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –NH-C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –$(CH_2)_r$–aryl substituted with one or more R_5, -O-C_{1-6} alkyl substituted with one or more R_5, –$(CH_2)_r$–C_{3-12} cycloalkyl substituted with one or more R_5, and –$(CH_2)_r$–4–10 membered heterocyclyl comprising carbon atoms and 1–5 heteroatoms selected from N, NR_6, O, and S and substituted with one or more R_5;

R_5 is independently selected from H, F, Cl, Br, CN, =O, C_{1-4} alkyl optionally substituted with one or more R_e, C_{2-4} alkenyl optionally substituted with one or more R_e, C_{2-4} alkynyl optionally substituted with one or more R_e, –$(CH_2)_rOR_b$, –$(CH_2)_rS(O)_pR_c$, –$(CH_2)_rS(O)_pNR_aR_a$, –$(CH_2)_rNR_aS(O)_pR_c$, –$(CH_2)_rNR_aR_a$, –$(CH_2)_rNR_aC(=O)R_b$, –$(CH_2)_rNR_aC(=O)OR_b$, –$(CH_2)_rNR_aC(=O)NR_aR_a$, –$(CH_2)_rC(=O)R_b$, –$(CH_2)_rC(=O)OR_b$, –$(CH_2)_rC(=O)NR_aR_a$, –$(CH_2)_rOC(=O)R_b$, –$(CH_2)_rOC(=O)OR_b$, –$(CH_2)_rO(CH_2)_rC(=O)NR_aR_a$, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_6 is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, -$S(O)_pR_c$, -$S(O)_pNR_aR_a$, -C(=O)R_b, –C(=O)OR_b, -C(=O)NR_aR_a, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_7 is independently selected from H, F, and Cl;

R_8 is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, and C_{3-6} cycloalkyl;

R_a is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more Re, C_{2-6} alkynyl optionally substituted with one or more R_e, $–(CH_2)_r–C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $–(CH_2)_r–$heterocyclyl optionally substituted with one or more R_e; or R_a and R_a together with the nitrogen atom to which they are both attached form a heterocyclic ring optionally substituted with one or more R_e;

R_b is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more R_e, C_{2-6} alkynyl optionally substituted with one or more R_e, $–(CH_2)_r–C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $–(CH_2)_r$ heterocyclyl optionally substituted with one or more R_e;

R_c is independently selected from C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more R_e, C_{2-6} alkynyl optionally substituted with one or more R_e, $–(CH_2)_r–C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $–(CH_2)_r–$heterocyclyl optionally substituted with one or more R_e;

R_d is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more R_e;

R_e is independently selected from F, Cl, Br, CN, NH_2, $–NH-C_{1-4}$ alkyl, $–N(C_{1-4}$ alkyl$)_2$, =O, OH, $-OC_{1-6}$ alkyl, $–CO_2H$, C_{1-6} alkyl optionally substituted with one or more R_f, C_{2-6} alkenyl, C_{2-6} alkynyl, $–(CH_2)_r–C_{3-6}$ cycloalkyl optionally substituted with one or more R_f, $–(CH_2)_r–$aryl optionally substituted with one or more R_f, and $–(CH_2)_r–$heterocyclyl optionally substituted with one or more R_f;

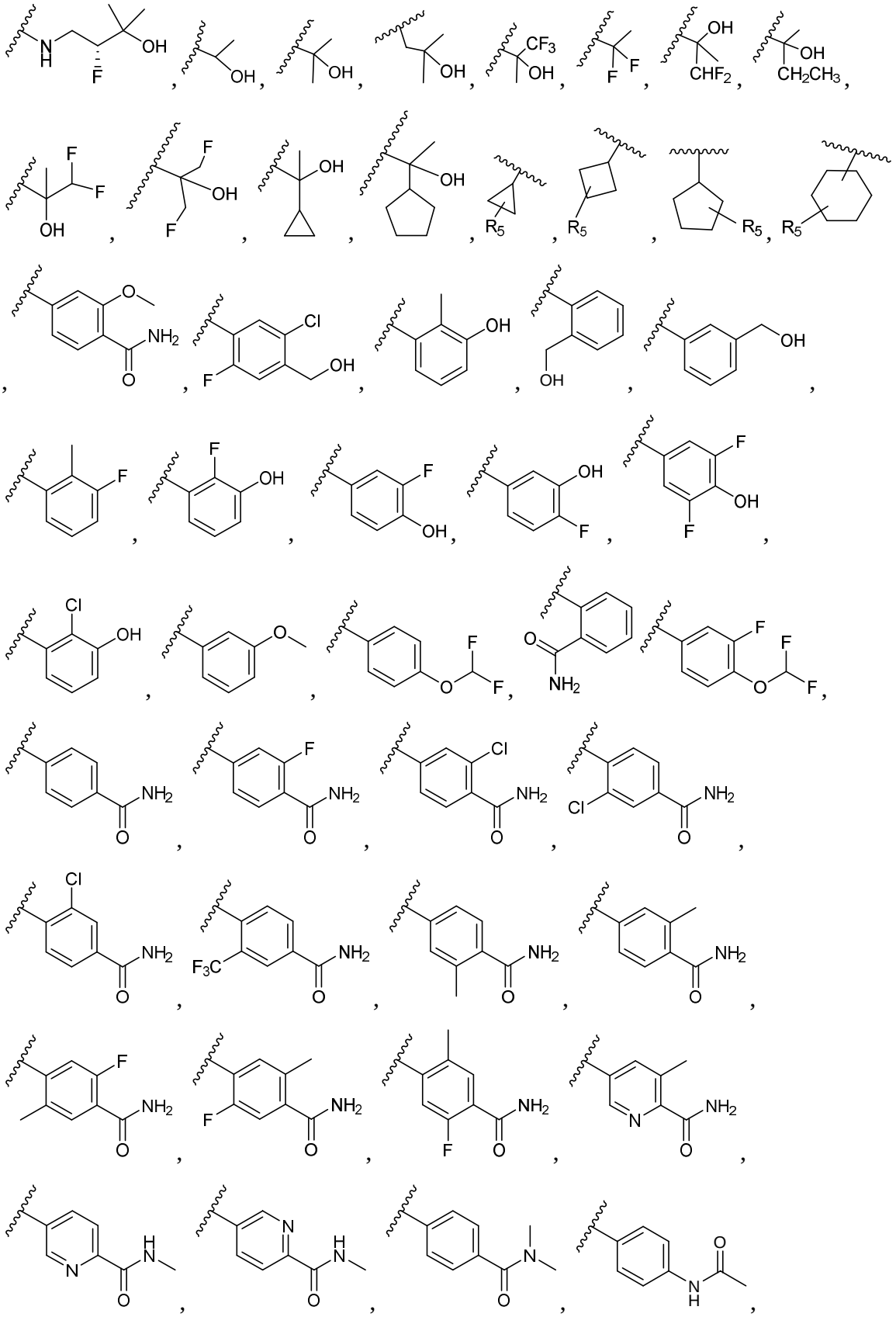
R_f is independently selected from F, Cl, Br, CN, OH, C_{1-5} alkyl optionally substituted with OH, C_{2-5} alkenyl, C_{2-5} alkynyl, C_{3-6} cycloalkyl, and phenyl;

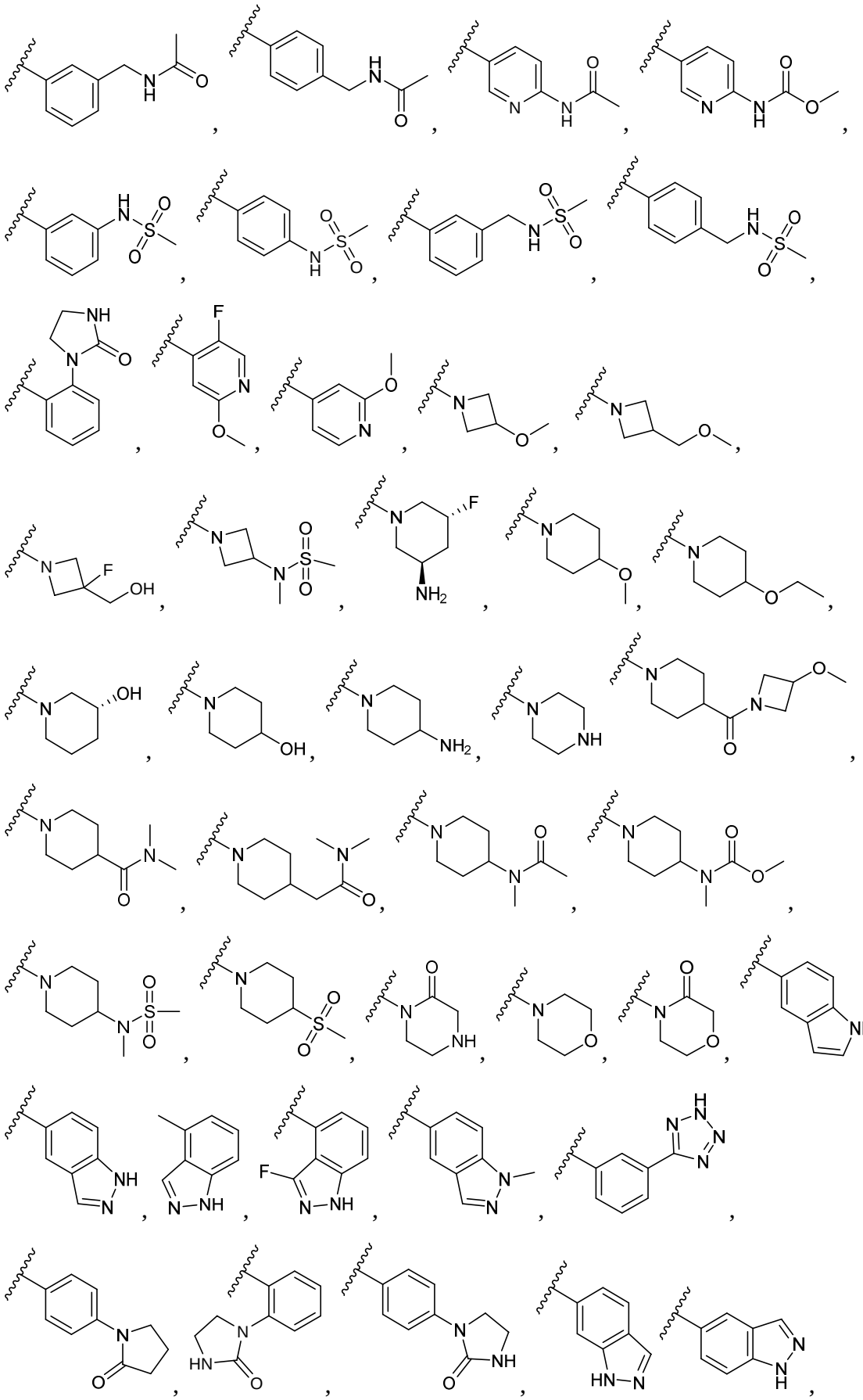
p, at each occurrence, is independently selected from zero, 1, and 2; and

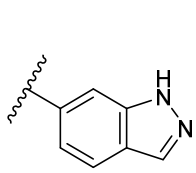
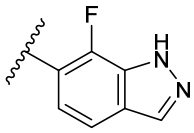
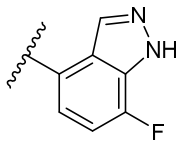
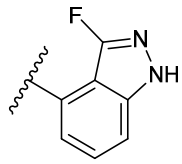
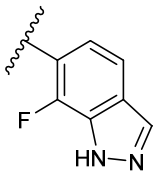
r, at each occurrence, is independently selected from zero, 1, 2, 3, and 4.

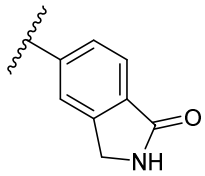
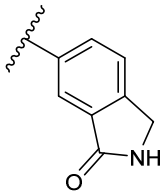
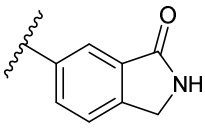
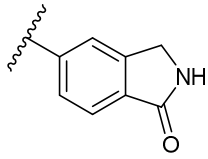
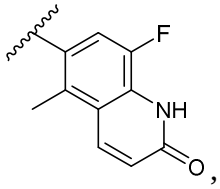
21. The compound according to any one of claims 16-19, or a pharmaceutically acceptable salt thereof, wherein;

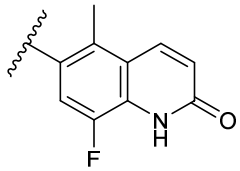
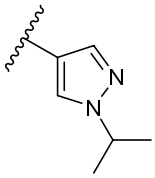
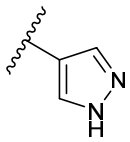
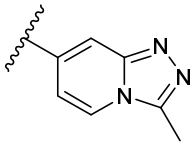
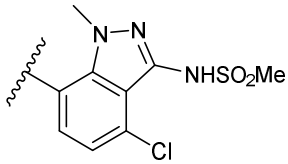
R_4 is independently selected from H, F, Cl, Br,

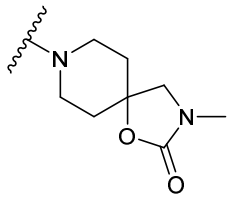
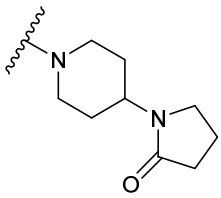
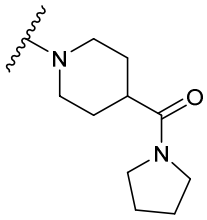
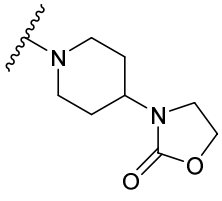


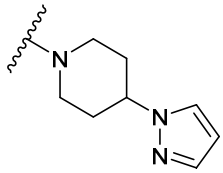


 ,  ,  ,  ,  ,

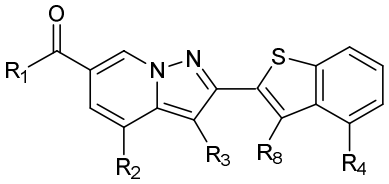
 ,  ,  ,  ,  ,

 ,  ,  ,  ,  ,

 ,  ,  ,  , and

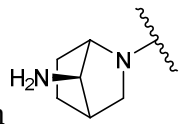
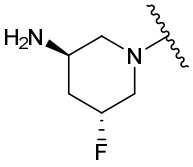
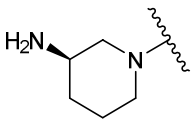
 .

22. The compound according to claim 1, having Formula (XIII):



(XIII)

or a pharmaceutically acceptable salt thereof, wherein:

R_1 is independently selected from  ,  , and  ;

R_2 is independently selected from H, F, CH_3, and OCH_3;

R_3 is independently selected from H, F, and CH_3;

R_4 is independently selected from H, F, Cl, Br, -C(=O)R_b, C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –NH-C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, OH, and C_{3-6} cycloalkyl, –$(CH_2)_r$–aryl substituted with one or more R_5, -O-C_{1-6} alkyl substituted with one or more R_5, –$(CH_2)_r$–C_{3-12} cycloalkyl substituted with one or more R_5, and –$(CH_2)_r$–4–10 membered heterocyclyl comprising carbon atoms and 1–5 heteroatoms selected from N, NR_6, O, and S and substituted with one or more R_5;

R_5 is independently selected from H, F, Cl, Br, CN, =O, C_{1-4} alkyl optionally substituted with one or more R_e, C_{2-4} alkenyl optionally substituted with one or more R_e, C_{2-4} alkynyl optionally substituted with one or more R_e, –$(CH_2)_rOR_b$, –$(CH_2)_rS(O)_pR_c$, –$(CH_2)_rS(O)_pNR_aR_a$, –$(CH_2)_rNR_aS(O)_pR_c$, –$(CH_2)_rNR_aR_a$, –$(CH_2)_rNR_aC(=O)R_b$, –$(CH_2)_rNR_aC(=O)OR_b$, –$(CH_2)_rNR_aC(=O)NR_aR_a$, –$(CH_2)_rC(=O)R_b$, –$(CH_2)_rC(=O)OR_b$, –$(CH_2)_rC(=O)NR_aR_a$, –$(CH_2)_rOC(=O)R_b$, –$(CH_2)_rOC(=O)OR_b$, –$(CH_2)_rO(CH_2)_rC(=O)NR_aR_a$, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_6 is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, -$S(O)_pR_c$, -$S(O)_pNR_aR_a$, -C(=O)R_b, –C(=O)OR_b, -C(=O)NR_aR_a, C_{3-6} cycloalkyl optionally substituted with one or more R_e, aryl optionally substituted with one or more R_e, and heterocyclyl optionally substituted with one or more R_e;

R_7 is independently selected from H, F, and Cl;

R_8 is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more substituents selected from F, Cl, and C_{3-6} cycloalkyl;

R_a is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more Re, C_{2-6} alkynyl optionally substituted with one or more R_e, –$(CH_2)_r$–C_{3-10} carbocyclyl optionally substituted with one or more R_e, and –$(CH_2)_r$–heterocyclyl optionally substituted with one or more R_e; or R_a and R_a together with the nitrogen atom to which they are both attached form a heterocyclic ring optionally substituted with one or more R_e;

R_b is independently selected from H, C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more R_e, C_{2-6} alkynyl optionally

substituted with one or more R_e, $-(CH_2)_r-C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $-(CH_2)_r$ heterocyclyl optionally substituted with one or more R_e;

R_c is independently selected from C_{1-6} alkyl optionally substituted with one or more R_e, C_{2-6} alkenyl optionally substituted with one or more R_e, C_{2-6} alkynyl optionally substituted with one or more R_e, $-(CH_2)_r-C_{3-10}$ carbocyclyl optionally substituted with one or more R_e, and $-(CH_2)_r-$heterocyclyl optionally substituted with one or more R_e;

R_d is independently selected from H, and C_{1-6} alkyl optionally substituted with one or more R_e;

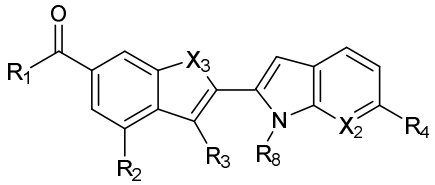
R_e is independently selected from F, Cl, Br, CN, NH_2, $-NH-C_{1-4}$ alkyl, $-N(C_{1-4}$ alkyl$)_2$, =O, OH, $-OC_{1-6}$ alkyl, $-CO_2H$, C_{1-6} alkyl optionally substituted with one or more R_f, C_{2-6} alkenyl, C_{2-6} alkynyl, $-(CH_2)_r-C_{3-6}$ cycloalkyl optionally substituted with one or more R_f, $-(CH_2)_r-$aryl optionally substituted with one or more R_f, and $-(CH_2)_r-$heterocyclyl optionally substituted with one or more R_f;

R_f is independently selected from F, Cl, Br, CN, OH, C_{1-5} alkyl optionally substituted with OH, C_{2-5} alkenyl, C_{2-5} alkynyl, C_{3-6} cycloalkyl, and phenyl;

p, at each occurrence, is independently selected from zero, 1, and 2; and

r, at each occurrence, is independently selected from zero, 1, 2, 3, and 4.

23. The compound according to claim 1, having Formula (XIV):

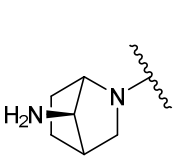


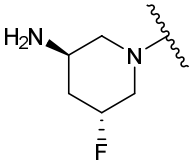
(XIV)

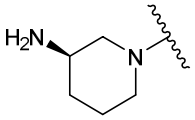
or a pharmaceutically acceptable salt thereof, wherein:

X_2 is independently selected from CR_4 and N;

X_3 is independently selected from O and S;

R_1 is independently selected from 

, 

, and 

;

R_2 is independently selected from CH_2OH, CH_2CH_2OH and OCH_3;

R_3 is independently selected from CH_2OH, CH_2CH_2OH, CH_2NH_2, $CH_2CH_2NH_2$, and $CH_2CH_2N_3$;

R_4 is independently selected from H and -O-C_{1-4} alkyl substituted with one or more R_5;

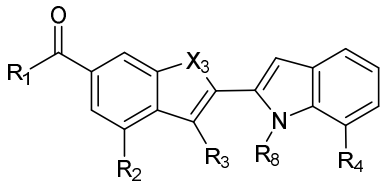
provided R_4 is not both -O-C_{1-4} alkyl substituted with one or more R_5;

R_5 is independently selected from OH and heterocyclyl optionally substituted with one or more R_e;

R_8 is independently selected from H, and C_{1-6} alkyl optionally substituted with C_{3-6} cycloalkyl; and

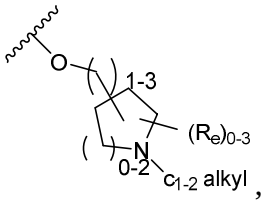
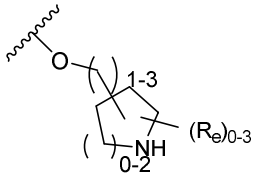
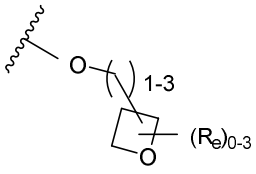
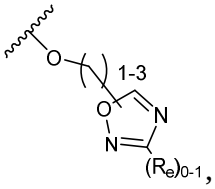
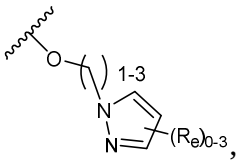
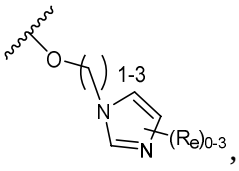
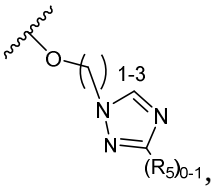
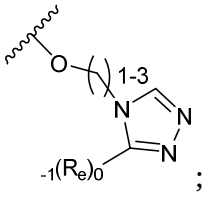
R_e is independently selected from NH_2 and C_{1-3} alkyl.

24. The compound according to claim 23, having Formula (XV):



(XV)

or a pharmaceutically acceptable salt thereof, wherein:

R_4 is independently selected from H, OCH_3, OCH_2CH_2OH,  ,  ,  ,  ,  ,  ,  , and  ;

R_8 is C_{1-3} alkyl substituted with C_{3-6} cycloalkyl; and

R_e is independently selected from NH_2 and C_{1-2} alkyl.

25. The compound according to claim 1, selected from:

5-(2-(6-((7R)-7-Amino-2-azabicyclo[2.2.1]- heptane-2-carbonyl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-b]pyridin-6-yl)isoindolin-1-one;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(6-cyclopropyl-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

5-(2-(6-((7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-6-yl)isoindolin-1-one;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-(3-methyl-[1,2,4]triazolo[4,3-a]pyridin-7-yl)-1H-indol-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-methyl-1H-indol-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

3((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-methyl-1H-pyrrolo[2,3-b]pyridin-2-yl)-4-fluoro-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

5-(2-(6-((7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-4-fluoro-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-b]pyridin-6-yl)isoindolin-1-one;

6-(2-(6-((7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-4-fluoro-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-b]pyridin-6-yl)isoindolin-1-one;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-(2-fluoro-3-hydroxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-4-fluoro-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-(3-methyl-[1,2,4]triazolo[4,3-a]pyridin-7-yl)-1H-indol-2-yl)-4-fluoro-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

6-(2-(6-((7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-b]pyridin-6-yl)isoindolin-1-one;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-(3-fluoro-4-hydroxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-(2-fluoro-3-hydroxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

4-(2-(6-((7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-b]pyridin-6-yl)-2-fluorobenzamide;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-(3-methyl-[1,2,4]triazolo[4,3-a]pyridin-7-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(6-cyclopropyl-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

6-(2-(6-((7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-6-yl)isoindolin-1-one;

5-(2-(6-((7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-6-yl)isoindolin-1-one;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-(2-hydroxypropan-2-yl)-1H-indol-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((3R,5R)-3-Amino-5-fluoropiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-(2-hydroxypropan-2-yl)-1H-indol-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-(2-hydroxypropan-2-yl)-1H-indol-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-(1,1,1-trifluoro-2-hydroxypropan-2-yl)-1H-indol-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-(2-hydroxypropan-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-(1,1,1-trifluoro-2-hydroxypropan-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-(1-hydroxyethyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(6-(4-aminopiperidin-1-yl)-1-(cyclopropylmethyl)-1H-indol-2-yl)-4-methoxy-3-methylbenzo[b]thiophen-6-yl)methanone;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(6-(4-aminopiperidin-1-yl)-1-(cyclopropylmethyl)-1H-indol-2-yl)-4-methoxy-3-methylbenzofuran-6-yl)methanone;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-(3-methyl-[1,2,4]triazolo[4,3-a]pyridin-7-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-3-methylbenzofuran-6-yl)methanonecyclopropylmethyl)-1H-indol-6-yl)isoindolin-1-one;

5-(2-(6-((7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-3-methylbenzofuran-2-yl)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-b]pyridin-6-yl)isoindolin-1-one;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-(3-methyl-[1,2,4]triazolo[4,3-a]pyridin-7-yl)-1H-indol-2-yl)-3-methylbenzofuran-6-yl)methanone;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-methyl-1H-indol-2-yl)-3-methylbenzofuran-6-yl)methanone;

4-(2-(6-((7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-3-methylbenzofuran-2-yl)-1-(cyclopropylmethyl)-1H-indol-6-yl)-2-fluorobenzamide;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-(2-methoxypyridin-4-yl)-1H-indol-2-yl)-3-methylbenzofuran-6-yl)methanone;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-(4-methoxypiperidin-1-yl)-1H-indol-2-yl)-3-methylbenzofuran-6-yl)methanone;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(6-(4-aminopiperidin-1-yl)-1-(cyclopropylmethyl)-1H-indol-2-yl)-3-methylbenzofuran-6-yl)methanone;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-(2-hydroxypropan-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-4-methoxy-3-methylbenzofuran-6-yl)methanone;

((7R)-7-Amino-2-azabicyclo[2.2.1]heptan-2-yl)(2-(1-(cyclopropylmethyl)-6-(2-hydroxypropan-2-yl)-1H-indol-2-yl)-3-methylbenzofuran-6-yl)methanone;

N-[5-(2-{6-[(3R,5R)-3-Amino-5-fluoropiperidine-1-carbonyl]-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-2-yl}-1-(cyclopropylmethyl)-1H-indol-6-yl)pyridin-2-yl]acetamide;

(3R,5R)-1-{2-[1-(Cyclopropylmethyl)-6-(4-methanesulfonylpiperidin-1-yl)-1H-indol-2-yl]-4-methoxy-3-methylpyrazolo[1,5-a]pyridine-6-carbonyl}-5-fluoropiperidin-3-amine;

3-(2-{6-[(7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl]-4-fluoro-3-methylpyrazolo[1,5-a]pyridin-2-yl}-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-b]pyridin-6-yl)-2-methylphenol;

5-(2-{6-[(7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl]-4-fluoro-3-methylpyrazolo[1,5-a]pyridin-2-yl}-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-b]pyridin-6-yl)-N-methylpyridine-2-carboxamide;

4-(2-{6-[(7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl]-4-fluoro-3-methylpyrazolo[1,5-a]pyridin-2-yl}-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-b]pyridin-6-yl)morpholin-3-one;

(7R)-2-{2-[1-(Cyclopropylmethyl)-6-(4-methanesulfonylpiperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl]-4-fluoro-3-methylpyrazolo[1,5-a]pyridine-6-carbonyl}-2-azabicyclo[2.2.1]heptan-7-amine;

(7R)-2-{2-[1-(Cyclopropylmethyl)-6-{3-methyl-[1,2,4]triazolo[4,3-a]pyridin-7-yl}-1H-indol-2-yl]-4-fluoro-3-methylpyrazolo[1,5-a]pyridine-6-carbonyl}-2-azabicyclo[2.2.1]heptan-7-amine;

(7R)-2-{2-[1-(Cyclopropylmethyl)-6-(1H-indazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl]-3-methylpyrazolo[1,5-a]pyridine-6-carbonyl}-2-azabicyclo[2.2.1]heptan-7-amine;

3-(2-{6-[(7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl]-3-methylpyrazolo[1,5-a]pyridin-2-yl}-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-b]pyridin-6-yl)-2-methylphenol;

1-[4-(2-{6-[(7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl]-3-methylpyrazolo[1,5-a]pyridin-2-yl}-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-b]pyridin-6-yl)phenyl]pyrrolidin-2-one;

4-(2-{6-[(7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl]-3-methylpyrazolo[1,5-a]pyridin-2-yl}-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-b]pyridin-6-yl)-2-fluoro-5-methylbenzamide;

(7R)-2-{2-[1-(Cyclopropylmethyl)-6-(7-fluoro-1H-indazol-6-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl]-3-methylpyrazolo[1,5-a]pyridine-6-carbonyl}-2-azabicyclo[2.2.1]heptan-7-amine;

Methyl N-[5-(2-{6-[(7R)-7-amino-2-azabicyclo[2.2.1]heptane-2-carbonyl]-3-methylpyrazolo[1,5-a]pyridin-2-yl}-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-b]pyridin-6-yl)pyridin-2-yl]carbamate;

4-(2-{6-[(7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl]-3-methylpyrazolo[1,5-a]pyridin-2-yl}-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-b]pyridin-6-yl)morpholin-3-one;

1-[4-(2-{6-[(7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl]-3-methylpyrazolo[1,5-a]pyridin-2-yl}-1-(cyclopropylmethyl)-1H-indol-6-yl)phenyl]pyrrolidin-2-one;

(7R)-2-{2-[1-(Cyclopropylmethyl)-6-(1H-indazol-6-yl)-1H-indol-2-yl]-3-methylpyrazolo[1,5-a]pyridine-6-carbonyl}-2-azabicyclo[2.2.1]heptan-7-amine;

(7R)-2-{2-[1-(Cyclopropylmethyl)-6-(1H-indazol-5-yl)-1H-indol-2-yl]-3-methylpyrazolo[1,5-a]pyridine-6-carbonyl}-2-azabicyclo[2.2.1]heptan-7-amine;

N-[7-(2-{6-[(7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl]-3-methylpyrazolo[1,5-a]pyridin-2-yl}-1-(cyclopropylmethyl)-1H-indol-6-yl)-4-chloro-1-methyl-1H-indazol-3-yl]methanesulfonamide;

1-[2-(2-{6-[(7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl]-3-methylpyrazolo[1,5-a]pyridin-2-yl}-1-(cyclopropylmethyl)-1H-indol-6-yl)phenyl]imidazolidin-2-one;

4-(2-{6-[(7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl]-3-methylpyrazolo[1,5-a]pyridin-2-yl}-1-(cyclopropylmethyl)-1H-indol-6-yl)-2-chlorobenzamide;

(7R)-2-{2-[1-(Cyclopropylmethyl)-6-(1H-pyrazol-4-yl)-1H-indol-2-yl]-3-methylpyrazolo[1,5-a]pyridine-6-carbonyl}-2-azabicyclo[2.2.1]heptan-7-amine;

(7R)-2-{2-[1-(Cyclopropylmethyl)-6-(morpholin-4-yl)-1H-indol-2-yl]-3-methylpyrazolo[1,5-a]pyridine-6-carbonyl}-2-azabicyclo[2.2.1]heptan-7-amine;

(3R,5R)-1-{2-[1-(Cyclopropylmethyl)-6-[4-(pyrrolidine-1-carbonyl)piperidin-1-yl]-1H-indol-2-yl]-3-methylpyrazolo[1,5-a]pyridine-6-carbonyl}-5-fluoropiperidin-3-amine;

3-[1-(2-{6-[(3R,5R)-3-Amino-5-fluoropiperidine-1-carbonyl]-3-methylpyrazolo[1,5-a]pyridin-2-yl}-1-(cyclopropylmethyl)-1H-indol-6-yl)piperidin-4-yl]-1,3-oxazolidin-2-one;

2-(2-{6-[(7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl]-3-methylpyrazolo[1,5-a]pyridin-2-yl}-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-b]pyridin-6-yl)-1,1-difluoropropan-2-ol;

2-(2-{6-[(7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl]-4-fluoro-3-methylpyrazolo[1,5-a]pyridin-2-yl}-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-b]pyridin-6-yl)-1,1,1-trifluoropropan-2-ol;

((3R,5R)-3-Amino-5-fluoropiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-(tetrahydro-2H-pyran-2-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((3R,5R)-3-Amino-5-fluoropiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-(3-hydroxycyclobutane-1-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((3R,5R)-3-Amino-5-fluoropiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-((1r,4r)-4-hydroxycyclohexane-1-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

(R)-(3-Aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-(3-hydroxycyclobutane-1-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((3R,5R)-3-Amino-5-fluoropiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-(tetrahydrofuran-2-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((3R,5R)-3-Amino-5-fluoropiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-(tetrahydrofuran-2-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

(R)-(3-Aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-(3-hydroxy-3-(trifluoromethyl)cyclobutane-1-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((3R,5R)-3-Amino-5-fluoropiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-(3-hydroxy-3-(trifluoromethyl)cyclobutane-1-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

(R)-1-(4-(2-(6-(3-Aminopiperidine-1-carbonyl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidin-1-yl)-2-methoxyethan-1-one;

(S)-1-(4-(2-(6-((3R,5R)-3-Amino-5-fluoropiperidine-1-carbonyl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidin-1-yl)-2-methoxypropan-1-one;

1-(4-(2-(6-((3R,5R)-3-Amino-5-fluoropiperidine-1-carbonyl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidin-1-yl)-2-methoxyethan-1-one;

((3R,5R)-3-Amino-5-fluoropiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-((1s,4s)-4-hydroxycyclohexane-1-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((R)-3-Aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-((1r,4r)-4-hydroxycyclohexane-1-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((3R,5R)-3-Amino-5-fluoropiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-((1r,4r)-4-hydroxycyclohexane-1-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

1-(4-(2-(6-((7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidin-1-yl)ethan-1-one;

(R)-1-(4-(2-(6-(3-Aminopiperidine-1-carbonyl)-4-fluoro-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidin-1-yl)ethan-1-one;

(R)-1-(4-(2-(6-((3R,5R)-3-Amino-5-fluoropiperidine-1-carbonyl)-4-fluoro-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidin-1-yl)-2-methoxypropan-1-one;

(R)-1-(4-(2-(6-((R)-3-Aminopiperidine-1-carbonyl)-4-fluoro-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidin-1-yl)-2-methoxypropan-1-one;

1-(4-(2-(6-((3R,5R)-3-Amino-5-fluoropiperidine-1-carbonyl)-4-fluoro-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidin-1-yl)ethan-1-one;

1-(4-(2-(6-((3R,5R)-3-Amino-5-fluoropiperidine-1-carbonyl)-4-fluoro-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidin-1-yl)-2-methoxyethan-1-one;

1-(4-(2-(6-((3R,5R)-3-amino-5-fluoropiperidine-1-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidin-1-yl)-2-hydroxyethan-1-one;

(R)-1-(4-(2-(6-(3-aminopiperidine-1-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidin-1-yl)-2-hydroxyethan-1-one;

1-(4-(2-(6-((3R,5R)-3-amino-5-fluoropiperidine-1-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidin-1-yl)-2-ethoxyethan-1-one;

((3R,5R)-3-amino-5-fluoropiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-((1s,4s)-4-hydroxycyclohexane-1-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((3R,5R)-3-amino-5-fluoropiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-((1R,3S)-3-hydroxycyclohexane-1-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((R)-3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-((1s,4s)-4-hydroxycyclohexane-1-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((3R,5R)-3-amino-5-fluoropiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-((1r,4r)-4-hydroxycyclohexane-1-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

1-(4-(2-(6-((3R,5R)-3-amino-5-fluoropiperidine-1-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidin-1-yl)ethan-1-one;

1-(4-(2-(6-((7R)-7-amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidin-1-yl)-2-methoxyethan-1-one;

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-(3-hydroxy-3-(trifluoromethyl)cyclobutane-1-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((R)-3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-(tetrahydro-2H-pyran-2-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

((R)-3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-(tetrahydrofuran-2-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

(4-(2-(6-((7R)-7-amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidin-1-yl)(3-hydroxycyclobutyl)methanone;

Methyl 4-(2-(6-((7R)-7-amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidine-1-carboxylate;

(2R)-1-(4-(2-(6-((7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidin-1-yl)-2-hydroxypropan-1-one;

(4-(2-(6-((7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidin-1-yl)(thiophen-2-yl)methanone;

1-(4-(2-(6-((3R,5R)-3-Amino-5-fluoropiperidine-1-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidin-1-yl)ethan-1-one;

1-(4-(2-(6-((7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)piperidin-1-yl)ethan-1-one;

1-(4-(2-(6-((3R,5R)-3-Amino-5-fluoropiperidine-1-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-5-fluoro-1H-indol-7-yl)piperidin-1-yl)-3-methylbutan-1-one;

((3R,5R)-3-Amino-5-fluoropiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-7-(1-(3-hydroxycyclobutane-1-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

(R)-1-(4-(2-(6-((R)-3-Aminopiperidine-1-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-5-fluoro-1H-indol-7-yl)piperidin-1-yl)-2-methoxypropan-1-one;

((R)-3-Aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-7-(1-(tetrahydro-2H-pyran-2-carbonyl)piperidin-4-yl)-1H-indol-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

1-(4-(2-(6-((3R,5R)-3-Amino-5-fluoropiperidine-1-carbonyl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-c]pyridin-7-yl)piperidin-1-yl)-2-methoxyethan-1-one;

((3R,5R)-3-Amino-5-fluoropiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-((1s,4s)-4-hydroxycyclohexane-1-carbonyl)azetidin-3-yl)-1H-indol-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

1-(3-(2-(6-((3R,5R)-3-Amino-5-fluoropiperidine-1-carbonyl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)azetidin-1-yl)-2-methoxyethan-1-one;

((R)-3-Aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-(1-((1r,4r)-4-hydroxycyclohexane-1-carbonyl)azetidin-3-yl)-1H-indol-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)methanone;

1-(3-(2-(6-((7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)azetidin-1-yl)ethan-1-one;

4-(((2-(6-((R)-3-Aminopiperidine-1-carbonyl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)oxy)methyl)pyrrolidin-2-one;

(R)-(2-(7-(2-(1H-1,2,4-Triazol-1-yl)ethoxy)-1-(cyclopropylmethyl)-1H-indol-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)(3-aminopiperidin-1-yl)methanone;

(2-(7-(2-(1H-1,2,4-Triazol-1-yl)ethoxy)-1-(cyclopropylmethyl)-1H-indol-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)((3R,5R)-3-amino-5-fluoropiperidin-1-yl)methanone;

(2-(7-(2-(4-Amino-1H-pyrazol-1-yl)ethoxy)-1-(cyclopropylmethyl)-1H-indol-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)((3R,5R)-3-amino-5-fluoropiperidin-1-yl)methanone;

4-(((2-(6-((R)-3-Aminopiperidine-1-carbonyl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)oxy)methyl)pyrrolidin-2-one;

4-(((2-(6-((3R,5R)-3-Amino-5-fluoropiperidine-1-carbonyl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)oxy)methyl)pyrrolidin-2-one;

4-(((2-(6-((R)-3-Aminopiperidine-1-carbonyl)-4-fluoro-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)oxy)methyl)pyrrolidin-2-one;

4-(((2-(6-((3R,5R)-3-Amino-5-fluoropiperidine-1-carbonyl)-4-fluoro-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)oxy)methyl)pyrrolidin-2-one;

(S)-5-(((2-(6-((R)-3-Aminopiperidine-1-carbonyl)-4-fluoro-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)oxy)methyl)pyrrolidin-2-one;

4-(((2-(6-((R)-3-Aminopiperidine-1-carbonyl)-4-fluoro-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)oxy)methyl)pyrrolidin-2-one;

(2-(7-(2-(1H-Imidazol-1-yl)ethoxy)-1-(cyclopropylmethyl)-1H-indol-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)((3R,5R)-3-amino-5-fluoropiperidin-1-yl)methanone;

(2-(7-(2-(1H-1,2,4-Triazol-1-yl)ethoxy)-1-(cyclopropylmethyl)-1H-indol-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)((3R,5R)-3-amino-5-fluoropiperidin-1-yl)methanone;

(S)-5-(((2-(6-((R)-3-Aminopiperidine-1-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)oxy)methyl)pyrrolidin-2-one;

4-(((2-(6-((3R,5R)-3-Amino-5-fluoropiperidine-1-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-indol-7-yl)oxy)methyl)pyrrolidin-2-one;

4-(((2-(6-((R)-3-Aminopiperidine-1-carbonyl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-c]pyridin-7-yl)oxy)methyl)pyrrolidin-2-one;

(2-(7-(2-(1H-1,2,4-Triazol-1-yl)ethoxy)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-c]pyridin-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)((3R,5R)-3-amino-5-fluoropiperidin-1-yl)methanone;

(2-(7-(2-(1H-Imidazol-1-yl)ethoxy)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-c]pyridin-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)((3R,5R)-3-amino-5-fluoropiperidin-1-yl)methanone;

(R)-(2-(7-(2-(1H-Imidazol-1-yl)ethoxy)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-c]pyridin-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)(3-aminopiperidin-1-yl)methanone;

(R)-(2-(7-(2-(4H-1,2,4-Triazol-4-yl)ethoxy)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-c]pyridin-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)(3-aminopiperidin-1-yl)methanone;

(2-(7-(2-(4H-1,2,4-Triazol-4-yl)ethoxy)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-c]pyridin-2-yl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-6-yl)((3R,5R)-3-amino-5-fluoropiperidin-1-yl)methanone;

4-(((2-(6-((3R,5R)-3-Amino-5-fluoropiperidine-1-carbonyl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-c]pyridin-7-yl)oxy)methyl)pyrrolidin-2-one;

4-(((2-(6-((3R,5R)-3-Amino-5-fluoropiperidine-1-carbonyl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-c]pyridin-7-yl)oxy)methyl)pyrrolidin-2-one;

(5R)-5-(((2-(6-((7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-c]pyridin-7-yl)oxy)methyl)pyrrolidin-2-one;

4-(((2-(6-((7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-c]pyridin-7-yl)oxy)methyl)pyrrolidin-2-one;

(5R)-5-(((2-(6-((7S)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-c]pyridin-7-yl)oxy)methyl)pyrrolidin-2-one;

4-(((2-(6-((7R)-7-Amino-2-azabicyclo[2.2.1]heptane-2-carbonyl)-4-methoxy-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-c]pyridin-7-yl)oxy)methyl)pyrrolidin-2-one;

(R)-(2-(7-(2-(4H-1,2,4-Triazol-4-yl)ethoxy)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-c]pyridin-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)(3-aminopiperidin-1-yl)methanone;

(2-(7-(2-(1H-Imidazol-1-yl)ethoxy)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-c]pyridin-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)((3R,5R)-3-amino-5-fluoropiperidin-1-yl)methanone;

(R)-(2-(7-(2-(1H-Imidazol-1-yl)ethoxy)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-c]pyridin-2-yl)-3-methylpyrazolo[1,5-a]pyridin-6-yl)(3-aminopiperidin-1-yl)methanone;

4-(((2-(6-((R)-3-Aminopiperidine-1-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-c]pyridin-7-yl)oxy)methyl)pyrrolidin-2-one;

4-(((2-(6-((R)-3-Aminopiperidine-1-carbonyl)-3-methylpyrazolo[1,5-a]pyridin-2-yl)-1-(cyclopropylmethyl)-1H-pyrrolo[2,3-c]pyridin-7-yl)oxy)methyl)pyrrolidin-2-one;

or a pharmaceutically acceptable salt thereof.

26. A pharmaceutical composition comprising a compound according to any one of the claims 1-25, or a stereoisomer, an enantiomer, a diastereomer, a tautomer, or a

pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable carriers.

27. Use of at least one compound according to any one of the claims 1-25 in the manufacture of a medicament~~A method~~ for treating a disease or a disorder associated with PAD4 enzyme activity, wherein ~~comprising administering to a subject in need of such treatment~~ a therapeutically effective amount of ~~at least one compound of according to any one of the claims 1-25~~the compound, or a stereoisomer, an enantiomer, a diastereomer, a tautomer, or a pharmaceutically acceptable salt thereof, is to be administered to a subject in need of such treatment.

28. Use of a composition according to claim 26 in the manufacture of a medicament ~~A method~~ for treating a disease or a disorder associated with PAD4 enzyme activity, wherein ~~comprising administering to a subject in need of such treatment~~ a therapeutically effective amount of the~~a~~ composition is to be administered to a subject in need of such treatment~~according to claim 26~~.

29. Use of a compound according to any one of claims 1-25, or a stereoisomer, an enantiomer, a diastereomer, a tautomer, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease or a disorder associated with PAD4 enzyme activity.

30. A compound according to any one of claims 1-25, or a stereoisomer, an enantiomer, a diastereomer, a tautomer, or a pharmaceutically acceptable salt thereof, for use in therapy.

31. The ~~method~~ use according to any one of claims 27~~-28~~ 29~~or the use according to claim 29~~, wherein the disease or the disorder associated with PAD4 enzyme activity is selected from rheumatoid arthritis, Alzheimer's disease, multiple sclerosis, lupus, Parkinson's disease, and cancer.