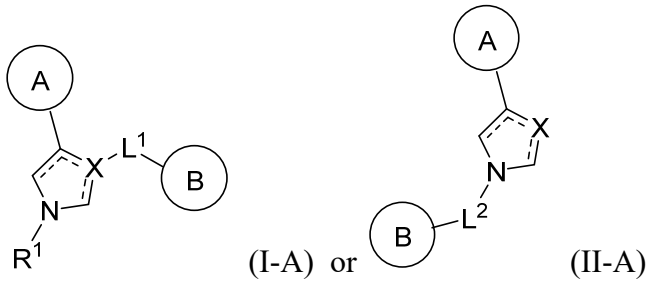
Claims:

Claim 1. A compound represented by Formula (I-A) or (II-A):



or a pharmaceutically acceptable salt and tautomer thereof, wherein:

each ═══ independently represents a single bond or a double bond;

X is N, NH, C, CH, or CH_2;

R^1 is H, C_{1-6}alkyl, cycloalkyl, heterocyclyl, -C(O)R^{1a}, –CH_2-aryl, -CH_2-heteroaryl, aryl, or heteroaryl; wherein R^{1a} is C_{1-6}alkyl; and wherein –CH_2-aryl, –CH_2-heteroaryl, aryl, and heteroaryl are optionally substituted with C_{1-6}alkyl or halo;

A is alkyl, cycloalkyl, heterocyclyl, a fused bicyclic aryl, a fused bicyclic heteroaryl, -CH_2-aryl, -CH_2-heteroaryl, aryl, or heteroaryl; wherein the aryl or heteroaryl is optionally substituted with aryl, heteroaryl, -Y^A-aryl, or –Y^A-heteroaryl; wherein Y^A is –O-, -C(O)-, -N(R^{A1})-, S(O)-, or –$S(O)_2$-; wherein R^{A1} is H or C_{1-6}alkyl;

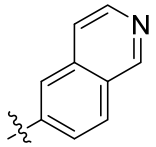
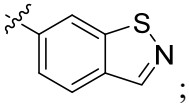
wherein the fused bicyclic aryl, the fused bicyclic heteroaryl, -CH_2-aryl, -CH_2-heteroaryl, each aryl, and each heteroaryl are optionally substituted with one or more substituents selected from the group consisting of alkyl, halo, haloalkyl, -CN, -N(R^A)$_2$, -OH, and -O-alkyl; wherein each R^A is independently H or C_{1-6}alkyl;

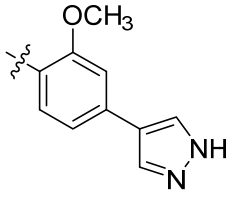
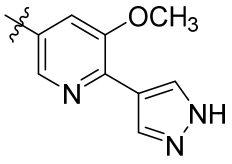
L^1 is –C(O)-NR^{L1}–, –O-C(S)-NR^{L1}–, –O-C(O)-NR^{L1}–, –NR^{L1}-C(O)–, –NR^{L1}-C(O)-O–, –NH-C(O)-NH–, –NR^{L1}-C(S)-NR^{L1}–, –NR^{L1}-$S(O)_2$–, –$S(O)_2$-NR^{L1}-, -CH_2-CH_2-, -CH_2-NR^{L1}-, -NR^{L1}-CH_2-, -CH_2-O-, -O-CH_2-, –O–, –NH–, –C(O)-azetidinyl, –CH_2-NR^{L1}-C(O)–, –C(O)-NR^{L1}-CH_2–, or -C(O)- ; wherein each R^{L1} is independently H or C_{1-6}alkyl; and

L^2 is –C(O)-NR^{L2}–, –$S(O)_2$-NR^{L2}-, -CH_2-CH_2-, –C(S)-NR^{L2}–, -C(O)-, or –$S(O)_2$–; wherein each R^{L2} is independently H or C_{1-6}alkyl; and

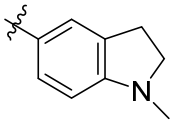
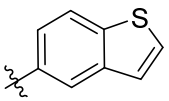
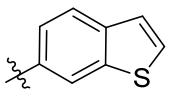
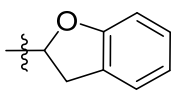
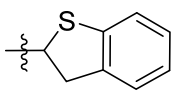
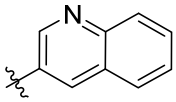
B is a fused bicyclic aryl, a fused bicyclic heteroaryl, -CH_2-aryl, -CH_2-heteroaryl, aryl, heteroaryl, cycloalkyl, –CH_2-heterocyclyl, or heterocyclyl, wherein the aryl, heteroaryl, cycloalkyl, or heterocyclyl is optionally substituted with aryl, heteroaryl, -Y^B-aryl, –Y^B-heteroaryl, –Y^B-heterocyclyl, or cycloalkyl; wherein Y^B is –O-, -CH_2-, -C(O)-, -N(R^{B1})-, -S(O)-, or –$S(O)_2$-; wherein R^{B1} is H or C_{1-6}alkyl;

wherein the fused bicyclic aryl, the fused bicyclic heteroaryl, -CH_2-aryl, -CH_2-heteroaryl, each aryl, each heteroaryl, each cycloalkyl, –CH_2-heterocyclyl, and each heterocyclyl are optionally substituted with one or more substituents selected from the group consisting of alkyl, halo, haloalkyl, -CN, -N(R^{B2})$_2$, -OH, -O-alkyl, and oxo; wherein each R^{B2} is independently H or C_{1-6}alkyl;

wherein when the compound is Formula (I-A); A is optionally substituted phenyl or thiophenyl, and L^1 is –C(O)-NH–; then B is not  or ;

wherein when the compound is Formula (I-A); A is phenyl, and L^1 is –C(O)-NH–; then B is not  or ;

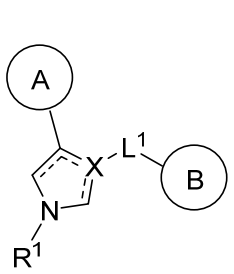
wherein when the compound is Formula (I-A); A is a substituted phenyl and B is a substituted phenyl, then L^1 is not –C(O)-NH–, –NH-C(O)–, –NCH_3-C(O)–, or –NH-C(O)-NH-;

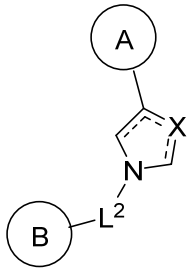
wherein when the compound is Formula (I-A); L^1 is –C(O)-NR^{L1}-CH_2– and B is an optionally substituted phenyl, substituted pyridyl, or ; then A is not substituted phenyl, substituted pyridyl, substituted thiophenyl, substituted thiazolyl, substituted pyrazolyl, , , , , or ;

wherein when the compound is Formula (I-A); B is optionally substituted -CH_2-aryl and A is optionally substituted aryl; then L^1 is not –C(O)-NH–;

wherein when the compound is Formula (II-A); A is optionally substituted phenyl and B is optionally substituted phenyl, then L^1 is not –C(O)-NCH_3–.

Claim 2. A compound of Formula (I) or (II):



(I) or


(II)

or a pharmaceutically acceptable salt or tautomer thereof, wherein:

each ⎓ independently represents a single bond or a double bond;

X is N, NH, C, CH, or CH_2;

R^1 is H, C_{1-6}alkyl, cycloalkyl, heterocyclyl, -C(O)R^{1a}, –CH_2-aryl, -CH_2-heteroaryl, aryl, or heteroaryl; wherein R^{1a} is C_{1-6}alkyl; and wherein –CH_2-aryl, –CH_2-heteroaryl, aryl, and heteroaryl are optionally substituted with C_{1-6}alkyl or halo;

A is alkyl, cycloalkyl, heterocyclyl, a fused bicyclic aryl, a fused bicyclic heteroaryl, -CH_2-aryl, -CH_2-heteroaryl, aryl, or heteroaryl; wherein the aryl or heteroaryl is optionally substituted with aryl, heteroaryl, -Y^A-aryl, or –Y^A-heteroaryl; wherein Y^A is –O-, -C(O)-, -N(R^{A1})-, -S(O)-, or –$S(O)_2$-; wherein R^{A1} is H or C_{1-6}alkyl;

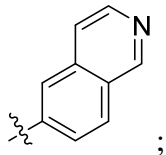
wherein the fused bicyclic aryl, the fused bicyclic heteroaryl, -CH_2-aryl, -CH_2-heteroaryl, each aryl, and each heteroaryl are optionally substituted with one or more substituents selected from the group consisting of alkyl, halo, -CN, -N(R^A)$_2$, -OH, and -O-alkyl; wherein each R^A is independently H or C_{1-6}alkyl;

L^1 is –C(O)-NR^{L1}–, –O-C(S)-NR^{L1}–, –O-C(O)-NR^{L1}–, –NR^{L1}-C(O)–, –NR^{L1}-C(O)-O–, –NH-C(O)-NH–, –NR^{L1}-C(S)-NR^{L1}–, –NR^{L1}-$S(O)_2$–, –$S(O)_2$-NR^{L1}-, -CH_2-CH_2-, -CH_2-NR^{L1}-, -NR^{L1}-CH_2-, -CH_2-O-, -O-CH_2-, –O–, –NH–, –C(O)-azetidinyl, –CH_2-NR^{L1}-C(O)–, or –C(O)-NR^{L1}-CH_2– ; wherein each R^{L1} is independently H or C_{1-6}alkyl; and

L^2 is –C(O)-NR^{L2}–, –$S(O)_2$-NR^{L2}-, -CH_2-CH_2-, –C(S)-NR^{L2}–, -C(O)-, or –$S(O)_2$–; wherein each R^{L2} is independently H or C_{1-6}alkyl; and

B is a fused bicyclic aryl, a fused bicyclic heteroaryl, -CH_2-aryl, -CH_2-heteroaryl, aryl, heteroaryl, cycloalkyl, or –CH_2-heterocyclyl, wherein the aryl or heteroaryl is optionally substituted with aryl, heteroaryl, -Y^B-aryl, or –Y^B-heteroaryl; wherein Y^B is –O-, -C(O)-, -N(R^{B1})-, -S(O)-, or –$S(O)_2$-; wherein R^{B1} is H or C_{1-6}alkyl;

wherein the fused bicyclic aryl, the fused bicyclic heteroaryl, -CH_2-aryl, -CH_2-heteroaryl, each aryl, each heteroaryl, cycloalkyl, and –CH_2-heterocyclyl are optionally substituted with one or more substituents selected from the group consisting of alkyl, halo, -CN, N(R^{B2})$_2$, -OH, and -O-alkyl; wherein each R^{B2} is independently H or C_{1-6}alkyl;

wherein when the compound is Formula (I); A is optionally substituted phenyl or thiophenyl, and L^1 is –C(O)-NH–; then B is not 

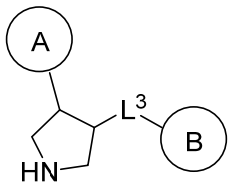
;

wherein when the compound is Formula (I); A is a substituted phenyl and B is a substituted phenyl, then L^1 is not –C(O)-NH–, –NH-C(O)–, –NCH_3-C(O)–, or –NH-C(O)-NH-;

wherein when the compound is Formula (I); B is optionally substituted -CH_2-aryl and A is optionally substituted aryl; then L^1 is not –C(O)-NH–;

wherein when the compound is Formula (II); A is optionally substituted phenyl and B is optionally substituted phenyl, then L^1 is not –C(O)-NCH_3–.

Claim 3. A compound of Formula (III):



(III)

or a pharmaceutically acceptable salt or tautomer thereof, wherein:

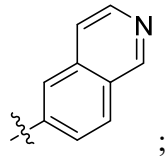
A is aryl or 5- to 6-membered heteroaryl, wherein the aryl and heteroaryl are optionally substituted with one or more substituents selected from the group consisting of alkyl, halo, -OH, and -O-alkyl;

L^3 is –C(O)-NR^{L3}–, –O-C(S)-NR^{L3}–, –O-C(O)-NR^{L3}–, –NR^{L3}-C(O)–, –NR^{L3}-C(S)-NR^{L3}–, –NR^{L3}-$S(O)_2$–, –$S(O)_2$-NR^{L3}-, -CH_2-CH_2-, -CH_2-NR^{L3}-, -NR^{L3}-CH_2-, -CH_2-O-, -O-CH_2-, or –O–; wherein each R^{L3} is independently hydrogen or C_{1-6}alkyl; and

B is a fused bicyclic aryl, a fused bicyclic heteroaryl, -CH_2-aryl, -CH_2-heteroaryl, aryl, or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with aryl or heteroaryl;

wherein the fused bicyclic aryl, the fused bicyclic heteroaryl, -CH_2-aryl, -CH_2-heteroaryl, each aryl, and each heteroaryl are optionally substituted with one or more substituents selected from the group consisting of alkyl, halo, -OH, and -O-alkyl;

wherein when A is optionally substituted phenyl or thiophenyl, and L^3 is –C(O)-NH–;

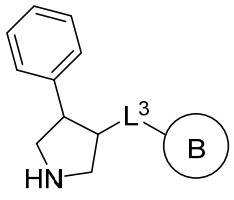
then B is not 

;

wherein when A is a substituted phenyl and B is a substituted phenyl, then L^3 is not –C(O)-NH–, –NH-C(O)–, or –NCH_3-C(O)–;

wherein when the compound is Formula (I); B is optionally substituted -CH_2-aryl and A is optionally substituted aryl; then L^3 is not –C(O)-NH–.

Claim 4. A compound of Formula (IV):



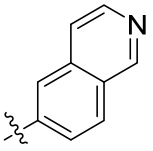
(IV)

or a pharmaceutically acceptable salt or tautomer thereof, wherein:

L^3 is –C(O)-NR^{L3}–, –O-C(S)-NR^{L3}–, –O-C(O)-NR^{L3}–, –NR^{L3}-C(O)–, –NR^{L3}-C(S)-NR^{L3}–, –NR^{L3}-$S(O)_2$–, –$S(O)_2$-NR^{L3}-, -CH_2-CH_2-, -CH_2-NR^{L3}-, -NR^{L3}-CH_2-, -CH_2-O-, -O-CH_2-, or –O–; wherein each R^{L3} is independently hydrogen or C_{1-6}alkyl; and

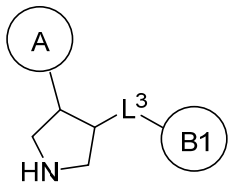
B is a fused bicyclic aryl, a fused bicyclic heteroaryl, -CH_2-aryl, -CH_2-heteroaryl, aryl, or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with aryl or heteroaryl;

wherein the fused bicyclic aryl, the fused bicyclic heteroaryl, -CH_2-aryl, -CH_2-heteroaryl, each aryl, and each heteroaryl are optionally substituted with one or more substituents selected from the group consisting of alkyl, halo, -OH, and -O-alkyl;

wherein when L^3 is –C(O)-NH–; then B is not 

.

Claim 5. A compound of Formula (V):



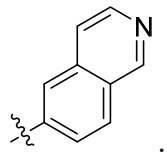
(V)

or a pharmaceutically acceptable salt or tautomer thereof, wherein:

A is aryl or 5- to 6-membered heteroaryl, wherein the aryl and heteroaryl are optionally substituted with one or more substituents selected from the group consisting of alkyl, halo, -OH, and -O-alkyl;

L^3 is –C(O)-NR^{L3}–, –O-C(S)-NR^{L3}–, –O-C(O)-NR^{L3}–, –NR^{L3}-C(O)–, –NR^{L3}-C(S)-NR^{L3}–, –NR^{L3}-$S(O)_2$–, –$S(O)_2$-NR^{L3}-, -CH_2-CH_2-, -CH_2-NR^{L3}-, -NR^{L3}-CH_2-, -CH_2-O-, -O-CH_2-, or –O–; wherein each R^{L3} is independently hydrogen or $C_{1\text{-}6}$alkyl; and

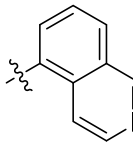
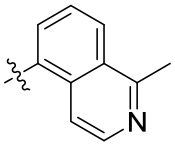
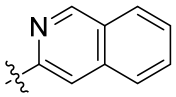
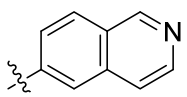
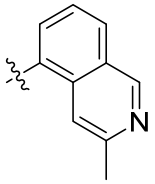
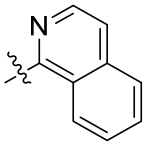
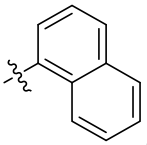
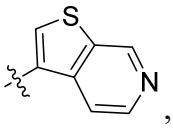
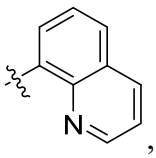
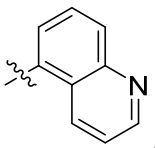
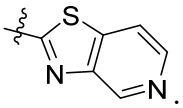
B1 is a fused bicyclic aryl or a fused bicyclic heteroaryl; wherein the fused bicyclic aryl and the fused bicyclic heteroaryl are optionally substituted with one or more substituents selected from the group consisting of alkyl, halo, -OH, and -O-alkyl;

wherein when A is optionally substituted phenyl or thiophenyl, and L^3 is –C(O)-NH–; then B is not 

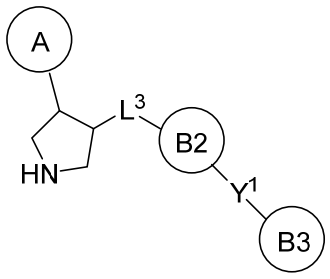
.

Claim 6. The compound of claim 5, or a pharmaceutically acceptable salt or tautomer thereof, wherein B1 is a fused bicyclic aryl.

Claim 7. The compound of claim 5, or a pharmaceutically acceptable salt or tautomer thereof, wherein B1 is a fused bicyclic heteroaryl.

Claim 8. The compound of claim 5, or a pharmaceutically acceptable salt or tautomer thereof, wherein B1 is selected from the group consisting of , , , , , , , , , , and .

Claim 9. A compound of Formula (VI):



(VI)

or a pharmaceutically acceptable salt or a tautomer thereof, wherein:

A is aryl or 5- to 6-membered heteroaryl, wherein the aryl and heteroaryl are optionally substituted with one or more substituents selected from the group consisting of alkyl, halo, -OH, and -O-alkyl;

L^3 is $–C(O)-NR^{L3}–$, $–O-C(S)-NR^{L3}–$, $–O-C(O)-NR^{L3}–$, $–NR^{L3}-C(O)–$, $–NR^{L3}-C(S)-NR^{L3}–$, $–NR^{L3}-S(O)_2–$, $–S(O)_2-NR^{L3}-$, $-CH_2-CH_2-$, $-CH_2-NR^{L3}-$, $-NR^{L3}-CH_2-$, $-CH_2-O-$, $-O-CH_2-$, or –O–; wherein each R^{L3} is independently hydrogen or C_{1-6}alkyl; and

B2 is monocyclic aryl or monocyclic heteroaryl; wherein the aryl and heteroaryl are optionally substituted with one or more substituents selected from the group consisting of alkyl, halo, -OH, and -O-alkyl;

Y^1 is absent, –O-, -C(O)-, $-N(R^Y)-$, -S(O)-, or $–S(O)_2-$; wherein R^Y is H or C_{1-6}alkyl; and

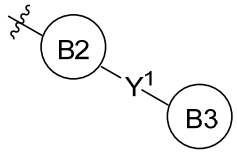
B3 is monocyclic aryl or monocyclic heteroaryl; wherein the aryl and heteroaryl are optionally substituted with one or more substituents selected from the group consisting of alkyl, halo, -OH, and -O-alkyl.

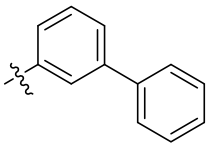
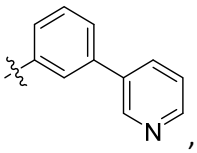
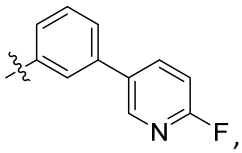
Claim 10. The compound of claim 9, or a pharmaceutically acceptable salt or tautomer thereof, wherein B2 is monocyclic aryl.

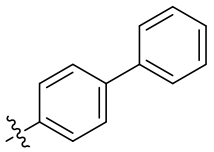
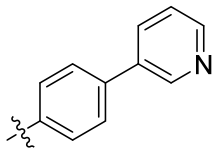
Claim 11. The compound of claim 9, or a pharmaceutically acceptable salt or tautomer thereof, wherein B2 is monocyclic heteroaryl.

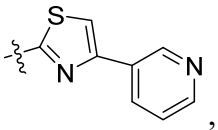
Claim 12. The compound of claim 9, or a pharmaceutically acceptable salt or tautomer thereof, wherein B3 is monocyclic aryl.

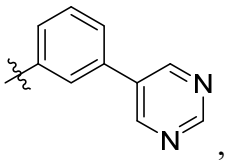
Claim 13. The compound of claim 9, or a pharmaceutically acceptable salt or tautomer thereof, wherein B3 is monocyclic heteroaryl.

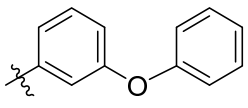
Claim 14. The compound of claim 9, or a pharmaceutically acceptable salt or tautomer thereof, wherein 

is selected from the group consisting of , , 

, , 

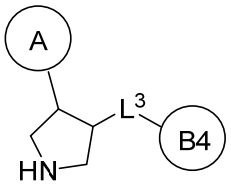
, 

, 

, and 

.

Claim 15. A compound of Formula (VII):



(VII)

or a pharmaceutically acceptable salt or tautomer thereof, wherein:

A is aryl or 5- to 6-membered heteroaryl, wherein the aryl and heteroaryl are optionally substituted with one or more substituents selected from the group consisting of alkyl, halo, -OH, and -O-alkyl;

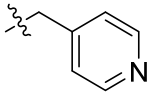
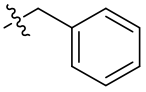
L^3 is –C(O)-NR^{L3}–, –O-C(S)-NR^{L3}–, –O-C(O)-NR^{L3}–, –NR^{L3}-C(O)–, –NR^{L3}-C(S)-NR^{L3}–, –NR^{L3}-$S(O)_2$–, –$S(O)_2$-NR^{L3}-, -CH_2-CH_2-, -CH_2-NR^{L3}-, -NR^{L3}-CH_2-, -CH_2-O-, -O-CH_2-, or –O–; wherein each R^{L3} is independently hydrogen or C_{1-6}alkyl; and

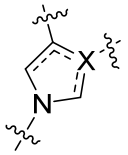
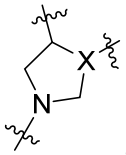
B4 is -CH_2-aryl or -CH_2-heteroaryl; wherein -CH_2-aryl and -CH_2-heteroaryl are optionally substituted with one or more substituents selected from the group consisting of alkyl, halo, -OH, and -O-alkyl;

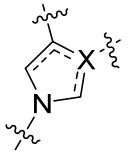
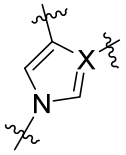
wherein when B4 is optionally substituted -CH_2-aryl and A is optionally substituted aryl; then L^3 is not –C(O)-NH–.

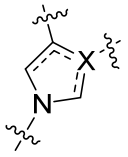
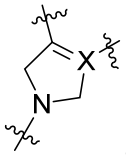
Claim 16. The compound of claim 15, or a pharmaceutically acceptable salt or tautomer thereof, wherein B4 is -CH_2-aryl.

Claim 17. The compound of claim 15, or a pharmaceutically acceptable salt or tautomer thereof, wherein B4 is -CH_2-heteroaryl.

Claim 18. The compound of claim 15, or a pharmaceutically acceptable salt or tautomer thereof, wherein B4 is selected from the group consisting of  and .

Claim 19. The compound of claim 1 or 2, or a pharmaceutically acceptable salt or tautomer thereof, wherein  is .

Claim 20. The compound of claim 1 or 2, or a pharmaceutically acceptable salt or tautomer thereof, wherein  is .

Claim 21. The compound of claim 1 or 2, or a pharmaceutically acceptable salt or tautomer thereof, wherein  is .

Claim 22. The compound of any one of claims 1-2 and 19-21, or a pharmaceutically acceptable salt or tautomer thereof, wherein X is N or NH.

Claim 23. The compound of any one of claims 1-2 and 19-21, or a pharmaceutically acceptable salt or tautomer thereof, wherein X is C, CH, or CH_2.

Claim 24. The compound of any one of claims 1-2 and 19-23, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^1 is H.

Claim 25. The compound of any one of claims 1-2 and 19-23, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^1 is $C_{1\text{-}6}$alkyl.

Claim 26. The compound of any one of claims 1-2 and 19-23, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^1 is cycloalkyl.

Claim 27. The compound of any one of claims 1-2 and 19-23, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^1 is heterocyclyl.

Claim 28. The compound of any one of claims 1-2 and 19-23, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^1 is -C(O)R^{1a}.

Claim 29. The compound of any one of claims 1-2 and 19-23, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^1 is –CH_2-aryl.

Claim 30. The compound of any one of claims 1-29, or a pharmaceutically acceptable salt thereof, wherein A is aryl.

Claim 31. The compound of claim 30, or a pharmaceutically acceptable salt or tautomer thereof, wherein the aryl is substituted with one or more substituents selected from the group consisting of alkyl, halo, -OH, and -O-alkyl.

Claim 32. The compound of any one of claims 1-29, or a pharmaceutically acceptable salt or tautomer thereof, wherein A is 5- to 6-membered heteroaryl.

Claim 33. The compound of claim 32, or a pharmaceutically acceptable salt or tautomer thereof, wherein the heteroaryl is substituted with one or more substituents selected from the group consisting of alkyl, halo, -OH, and -O-alkyl.

Claim 34. The compound of any one of claims 1-29, or a pharmaceutically acceptable salt or tautomer thereof, wherein A is alkyl.

Claim 35. The compound of any one of claims 1-29, or a pharmaceutically acceptable salt or tautomer thereof, wherein A is cycloalkyl.

Claim 36. The compound of any one of claims 1-29, or a pharmaceutically acceptable salt or tautomer thereof, wherein A is heterocyclyl.

Claim 37. The compound of any one of claims 1-29, or a pharmaceutically acceptable salt or tautomer thereof, wherein A is a fused bicyclic aryl or a fused bicyclic heteroaryl.

Claim 38. The compound of any one of claims 1-29, or a pharmaceutically acceptable salt or tautomer thereof, wherein A is -CH_2-aryl or -CH_2-heteroaryl.

Claim 39. The compound of any one of claims 1-2 and 18-38, or a pharmaceutically acceptable salt or tautomer thereof, wherein L^1 is –C(O)-NR^{L1}–.

Claim 40. The compound of any one of claims 1-2 and 18-38, or a pharmaceutically acceptable salt or tautomer thereof, wherein L^1 is –O-C(S)-NR^{L1}–.

Claim 41. The compound of any one of claims 1-2 and 18-38, or a pharmaceutically acceptable salt or tautomer thereof, wherein L^1 is –O-C(O)-NR^{L1}–.

Claim 42. The compound of any one of claims 1-2 and 18-38, or a pharmaceutically acceptable salt or tautomer thereof, wherein L^1 is –NR^{L1}-C(S)-NR^{L1}–.

Claim 43. The compound of any one of claims 1-2 and 18-38, or a pharmaceutically acceptable salt or tautomer thereof, wherein L^1 is –O–.

Claim 44. The compound of any one of claims 1-2 and 18-38, or a pharmaceutically acceptable salt or tautomer thereof, wherein L^1 is –NR^{L1}-C(O)–, –NR^{L1}-C(O)-O–, –NH-C(O)-NH–, –NR^{L1}-$S(O)_2$– or –$S(O)_2$-NR^{L1}-.

Claim 45. The compound of any one of claims 1-2 and 18-38, or a pharmaceutically acceptable salt or tautomer thereof, wherein L^1 is -CH_2-CH_2-, -CH_2-NR^{L1}-, -NR^{L1}-CH_2-, -CH_2-O-, -O-CH_2-, –NH–, or –C(O)-azetidinyl.

Claim 46. The compound of any one of claims 1-2 and 18-38, or a pharmaceutically acceptable salt or tautomer thereof, wherein L^2 is –C(O)-NR^{L2}–.

Claim 47. The compound of any one of claims 1-2 and 18-38, or a pharmaceutically acceptable salt or tautomer thereof, wherein L^2 is –$S(O)_2$-NR^{L2}- or -CH_2-CH_2-.

Claim 48. The compound of any one of claims 3-18 and 30-38, or a pharmaceutically acceptable salt or tautomer thereof, wherein L^3 is –C(O)-NR^{L3}–.

Claim 49. The compound of any one of claims 3-18 and 30-38, or a pharmaceutically acceptable salt or tautomer thereof, wherein L^3 is –O-C(S)-NR^{L3}–.

Claim 50. The compound of any one of claims 3-18 and 30-38, or a pharmaceutically acceptable salt or tautomer thereof, wherein L^3 is –O-C(O)-NR^{L3}–.

Claim 51. The compound of any one of claims 3-18 and 30-38, or a pharmaceutically acceptable salt or tautomer thereof, wherein L^3 is – NR^{L3}-C(S)-NR^{L3}–.

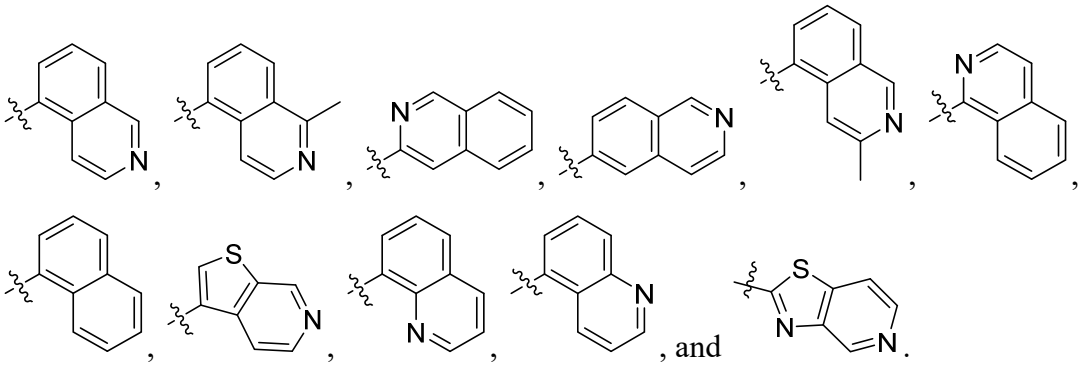
Claim 52. The compound of any one of claims 3-18 and 30-38, or a pharmaceutically acceptable salt or tautomer thereof, wherein L^3 is –NR^{L3}-C(O)–, –NR^{L3}-$S(O)_2$–, –$S(O)_2$-NR^{L3}-, -CH_2-CH_2-, -CH_2-NR^{L3}-, or -NR^{L3}-CH_2-.

Claim 53. The compound of any one of claims 3-18 and 30-38, or a pharmaceutically acceptable salt or tautomer thereof, wherein L^3 is -CH_2-O-, -O-CH_2-, or –O–.

Claim 54. The compound of any one of claims 1-4 and 19-53, or a pharmaceutically acceptable salt or tautomer thereof, wherein B is a fused bicyclic aryl.

Claim 55. The compound of any one of claims 1-4 and 19-53, or a pharmaceutically acceptable salt or tautomer thereof, wherein B is a fused bicyclic heteroaryl.

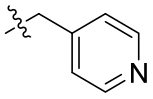
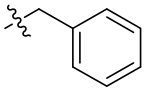
Claim 56. The compound of any one of claims 1-4 and 19-53, or a pharmaceutically acceptable salt or tautomer thereof, wherein B is selected from the group consisting of



, and .

Claim 57. The compound of any one of claims 1-4 and 19-53, or a pharmaceutically acceptable salt or tautomer thereof, wherein B is -CH_2-aryl.

Claim 58. The compound of any one of claims 1-4 and 19-53, or a pharmaceutically acceptable salt or tautomer thereof, wherein B is -CH_2-heteroaryl.

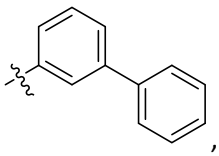
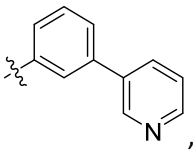
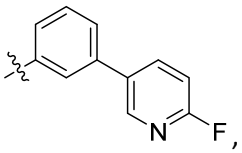
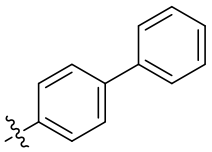
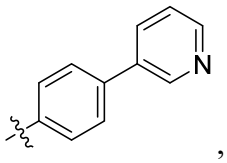
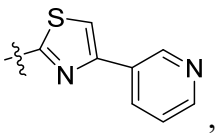
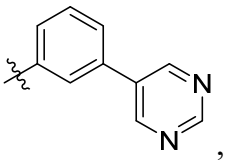
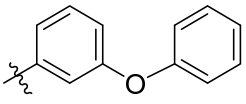
Claim 59. The compound of any one of claims 1-4 and 19-53, or a pharmaceutically acceptable salt or tautomer thereof, wherein B is selected from the group consisting of  and .

Claim 60. The compound of any one of claims 1-4 and 19-52, or a pharmaceutically acceptable salt or tautomer thereof, wherein B is aryl.

Claim 61. The compound of any one of claims 1-4 and 19-52, or a pharmaceutically acceptable salt or tautomer thereof, wherein B is aryl substituted with aryl or heteroaryl.

Claim 62. The compound of any one of claims 1-4 and 19-52, or a pharmaceutically acceptable salt or tautomer thereof, wherein B is heteroaryl.

Claim 63. The compound of any one of claims 1-4 and 19-52, or a pharmaceutically acceptable salt or tautomer thereof, wherein B is heteroaryl substituted with aryl or heteroaryl.

Claim 64. The compound of any one of claims 1-4 and 19-52, or a pharmaceutically acceptable salt or tautomer thereof, wherein B is selected from the group consisting of , , , , , , , and .

Claim 65. The compound of any one of claims 1-4 and 19-52, or a pharmaceutically acceptable salt or tautomer thereof, wherein B is cycloalkyl.

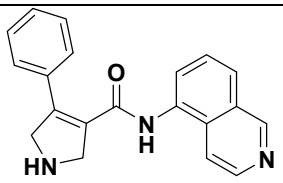
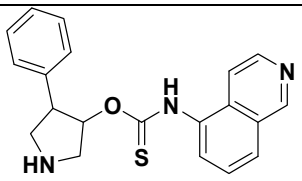
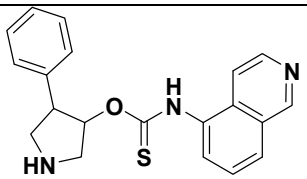
Claim 66. The compound of any one of claims 1-4 and 19-52, or a pharmaceutically acceptable salt or tautomer thereof, wherein B is cycloalkyl substituted with aryl, heteroaryl, -Y^B-aryl, –Y^B-heteroaryl.

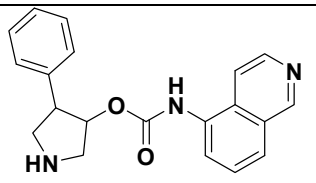
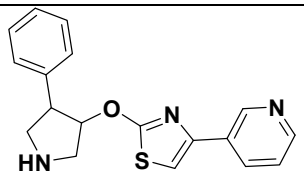
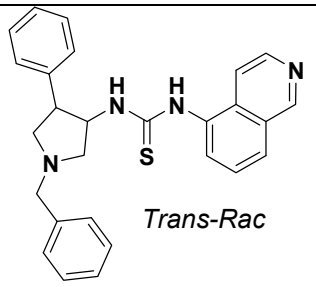
Claim 67. The compound of any one of claims 1-4 and 19-52, or a pharmaceutically acceptable salt or tautomer thereof, wherein B is –CH_2-heterocyclyl.

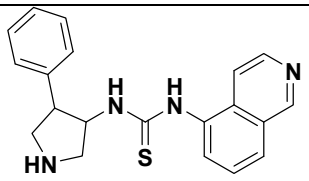
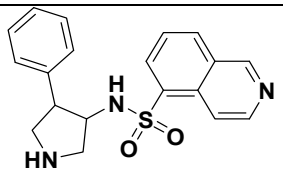
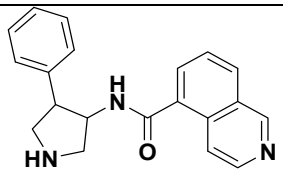
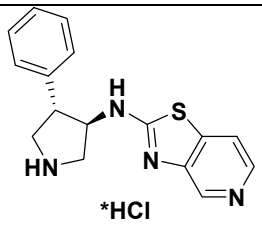
Claim 68. The compound of any one of claims 1-4 and 19-52, or a pharmaceutically acceptable salt or tautomer thereof, wherein B is heterocyclyl.

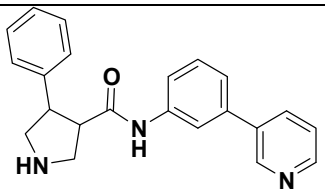
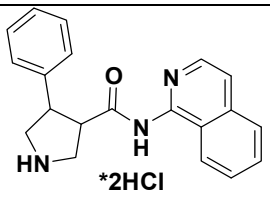
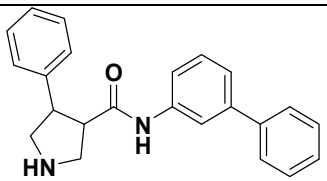
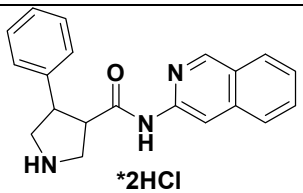
Claim 69. The compound of any one of claims 1-4 and 19-52, or a pharmaceutically acceptable salt or tautomer thereof, wherein B is heterocyclyl substituted with aryl or heteroaryl.

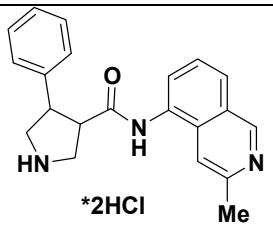
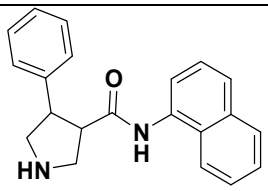
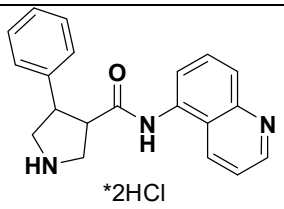
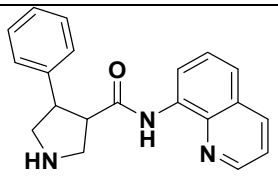
Claim 70. A compound, or a pharmaceutically acceptable salt or tautomer thereof, selected from the group consisting of

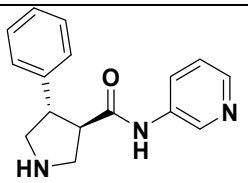
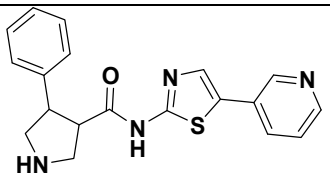
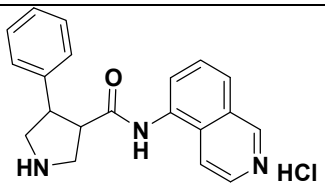
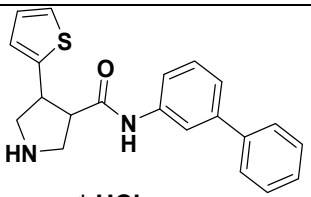
Compound No.	Structure
I-1	 *N*-(isoquinolin-5-yl)-4-phenyl-2,5-dihydro-1*H*-pyrrole-3-carboxamide
I-2	 *Trans-Rac* *(±)-trans-O*-(4-phenylpyrrolidin-3-yl) isoquinolin-5-ylcarbamothioate
I-3	 *Cis-Rac* *(±)-cis-O*-(4-phenylpyrrolidin-3-yl) isoquinolin-5-ylcarbamothioate

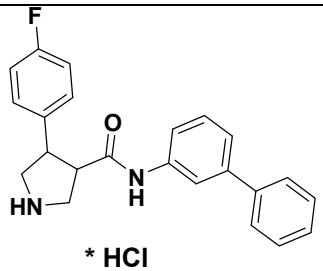
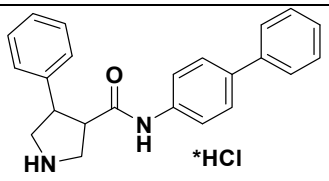
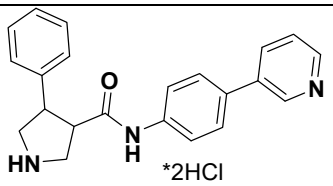
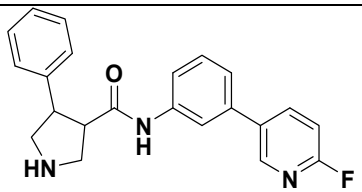
Compound No.	Structure
I-4	 *Trans-Rac* *(±)-trans*-4-phenylpyrrolidin-3-yl isoquinolin-5-ylcarbamate
I-5	 *Trans-Rac* *(±)-trans*-3-{2-[(4-phenylpyrrolidin-3-yl)oxy]-1,3-thiazol-4-yl}pyridine
I-6	 *Trans-Rac* *(±)-trans*-1-isoquinolin-5-yl-3-(1-benzyl-4-phenylpyrrolidin-3-yl)thioure

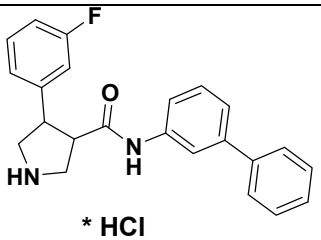
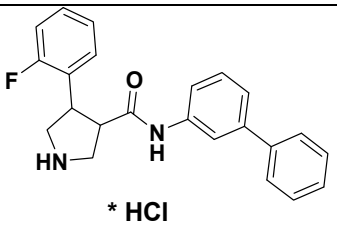
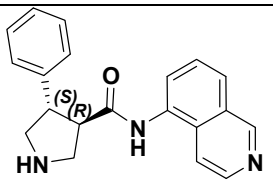
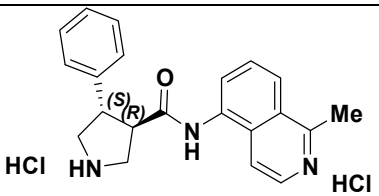
Compound No.	Structure
I-7	 *Trans-Rac* *(±)-trans*-1-isoquinolin-5-yl-3-(4-phenylpyrrolidin-3-yl)thiourea
I-8	 *Trans-Rac* *(±)-trans-N*-(4-phenylpyrrolidin-3-yl)isoquinoline-5-sulfonamide
I-9	 *Trans-Rac* *(±)-trans-N*-(4-phenylpyrrolidin-3-yl)isoquinoline-5-carboxamide
I-10	 *Trans-Rac* *(±)-trans-N*-[4-phenylpyrrolidin-3-yl][1,3]thiazolo[4,5-*c*]pyridin-2-amine hydrochloride

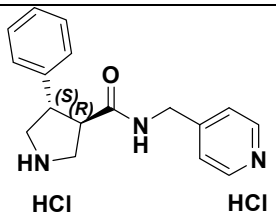
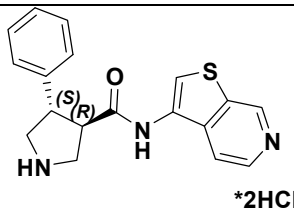
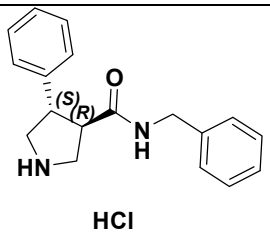
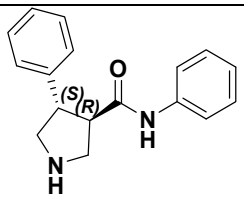
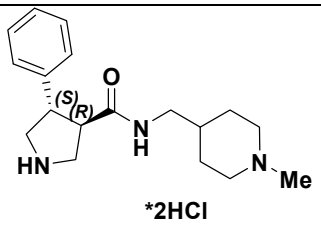
Compound No.	Structure
I-11	 *Trans-Racemate* *(±)-trans*-4-phenyl-*N*-[3-(pyridin-3-yl)phenyl]pyrrolidine-3-carboxamide
I-12	 *Trans-Rac* *(±)-trans-N*-(isoquinolin-1-yl)-4-phenylpyrrolidine-3-carboxamide dihydrochloride
I-13	 *Trans-Rac* *(±)-trans-N*-(biphenyl-3-yl)-4-phenylpyrrolidine-3-carboxamide
I-14	 *Trans-Rac* *(±)-trans-N*-(isoquinolin-3-yl)-4-phenylpyrrolidine-3-carboxamide dihydrochloride

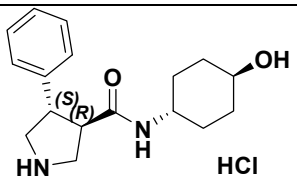
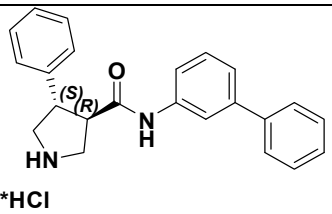
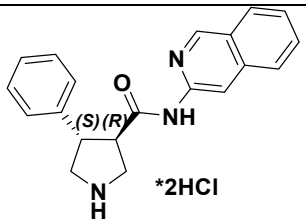
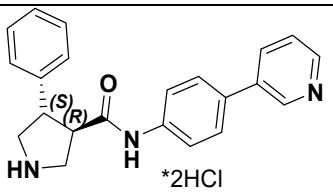
Compound No.	Structure
I-15	 *2HCl Me *Trans-Rac* *(±)-trans-N*-(3-methylisoquinolin-5-yl)-4-phenylpyrrolidine-3-carboxamide dihydrochloride
I-16	 HCl *Trans-Rac* *(±)-trans-N*-(naphthalen-1-yl)-4-phenylpyrrolidine-3-carboxamide hydrochloride
I-17	 *2HCl *Trans-Rac* *(±)-trans*-4-phenyl-*N*-(quinolin-5-yl)pyrrolidine-3-carboxamide dihydrochloride
I-18	 * 2HCl *Trans-Rac* *(±)-trans*-4-phenyl-*N*-(quinolin-8-yl)pyrrolidine-3-carboxamide dihydrochloride

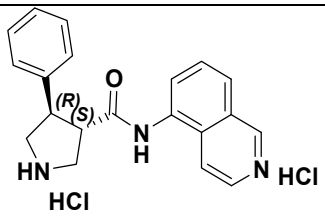
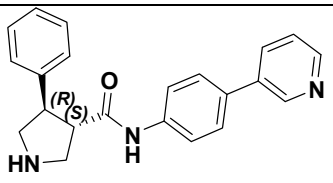
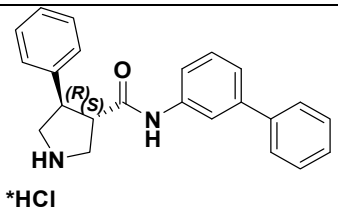
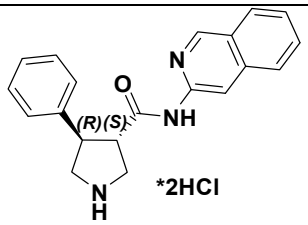
Compound No.	Structure
I-19	 *Trans-Rac* *(±)-trans*-4-phenyl-*N*-(pyridin-3-yl)pyrrolidine-3-carboxamide dihydrochloride
I-20	 *Trans-Rac* *(±)-trans*-4-phenyl-*N*-[5-(pyridin-3-yl)-1,3-thiazol-2-yl]pyrrolidine-3-carboxamide
I-21	 HCl HCl *Trans-Rac* *(±)-trans-N*-(isoquinolin-5-yl)-4-phenylpyrrolidine-3-carboxamide dihydrochloride
I-22	 * HCl *Trans- Rac* *(±)-trans-N*-(biphenyl-3-yl)-4-(thiophen-2-yl)pyrrolidine-3-carboxamide hydrochloride

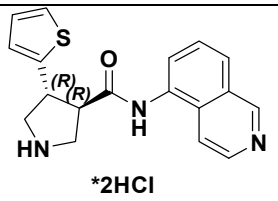
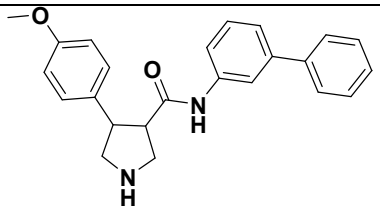
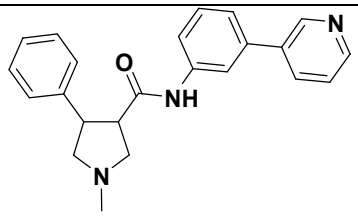
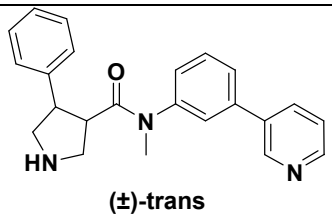
Compound No.	Structure
I-23	 * HCl *Trans- Rac* *(±)-trans-N*-(biphenyl-3-yl)-4-(4-fluorophenyl)pyrrolidine-3-carboxamide hydrochloride
I-24	 *Trans-Rac* *(±)-trans-N*-(biphenyl-4-yl)-4-phenylpyrrolidine-3-carboxamide hydrochloride
I-25	 *Trans-Rac* *(±)-trans*-4-phenyl-*N*-[4-(pyridin-3-yl)phenyl]pyrrolidine-3-carboxamide dihydrochloride
I-26	 *Trans-Rac* *(±)-trans-N*-[3-(6-fluoropyridin-3-yl)phenyl]-4-phenylpyrrolidine-3-carboxamide

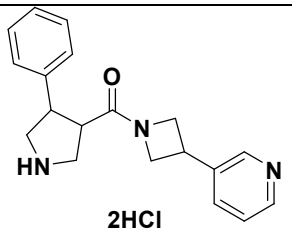
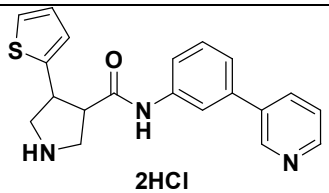
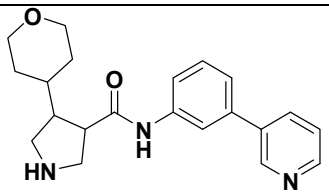
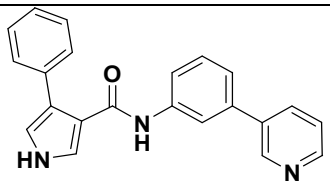
Compound No.	Structure
I-27	 * HCl *Trans- Rac* *(±)-trans-N*-(biphenyl-3-yl)-4-(3-fluorophenyl)pyrrolidine-3-carboxamide hydrochloride
I-28	 * HCl *Trans- Rac* *(±)-trans-N*-(biphenyl-3-yl)-4-(2-fluorophenyl)pyrrolidine-3-carboxamide hydrochloride
I-29	 (3*R*,4*S*)-*N*-(isoquinolin-5-yl)-4-phenylpyrrolidine-3-carboxamide
I-30	 (3*R*,4*S*)-*N*-(1-methylisoquinolin-5-yl)-4-phenylpyrrolidine-3-carboxamide dihydrochloride

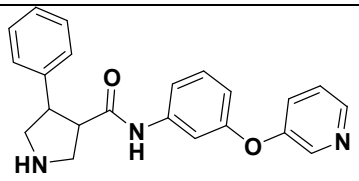
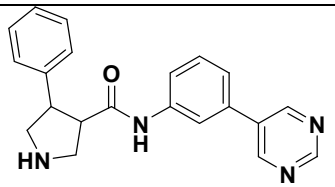
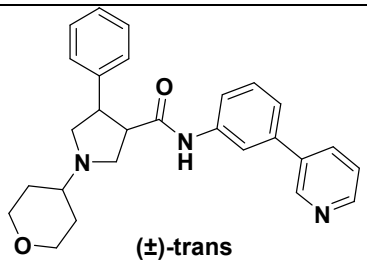
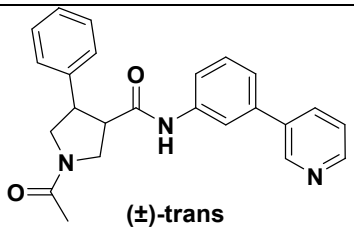
Compound No.	Structure
I-31	 (3*R*,4*S*)-4-phenyl-*N*-(pyridin-4-ylmethyl)pyrrolidine-3-carboxamide dihydrochloride
I-32	 (3*R*,4*S*)-4-phenyl-*N*-(thieno[2,3-*c*]pyridin-3-yl)pyrrolidine-3-carboxamide dihydrochloride
I-33	 (3*R*,4*S*)-*N*-benzyl-4-phenylpyrrolidine-3-carboxamide hydrochloride
I-34	 (3*R*,4*S*)-*N*,4-diphenylpyrrolidine-3-carboxamide
I-35	 *2HCl

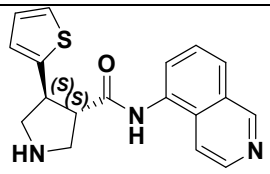
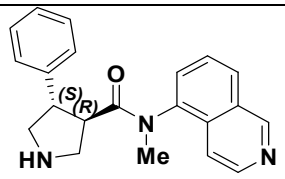
Compound No.	Structure
	(3*R*,4*S*)-*N*-[(1-methylpiperidin-4-yl)methyl]-4-phenylpyrrolidine-3-carboxamide dihydrochloride
I-36	 (3*R*,4*S*)-*N*-[(*1,4-trans*)-4-hydroxycyclohexyl]-4-phenylpyrrolidine-3-carboxamide hydrochloride
I-37	 (3*R*,4*S*)-*N*-(biphenyl-3-yl)-4-phenylpyrrolidine-3-carboxamide hydrochloride
I-38	 (3*R*,4*S*)-*N*-(isoquinolin-3-yl)-4-phenylpyrrolidine-3-carboxamide dihydrochloride
I-39	 (3*R*,4*S*)-4-phenyl-*N*-[4-(pyridin-3-yl)phenyl]pyrrolidine-3-carboxamide dihydrochloride

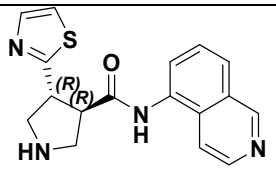
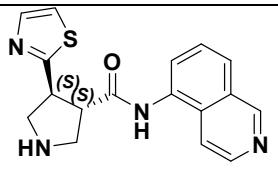
Compound No.	Structure
I-40	 (3*S*,4*R*)-*N*-(isoquinolin-5-yl)-4-phenylpyrrolidine-3-carboxamide dihydrochloride
I-41	 (3*S*,4*R*)-4-phenyl-*N*-[4-(pyridin-3-yl)phenyl]pyrrolidine-3-carboxamide dihydrochloride
I-42	 (3*S*,4*R*)-*N*-(biphenyl-3-yl)-4-phenylpyrrolidine-3-carboxamide hydrochloride
I-43	 (3*S*,4*R*)-*N*-(isoquinolin-3-yl)-4-phenylpyrrolidine-3-carboxamide dihydrochloride

Compound No.	Structure
I-44	 (3*R*,4*R*)-*N*-(isoquinolin-5-yl)-4-(thiophen-2-yl)pyrrolidine-3-carboxamide dihydrochloride
I-45	 *(±)-trans*-*N*-(biphenyl-3-yl)-4-(4-methoxyphenyl)pyrrolidine-3-carboxamide hydrochloride
I-46	 *(±)-trans*-1-methyl-4-phenyl-*N*-[3-(pyridin-3-yl)phenyl]pyrrolidine-3-carboxamide
I-47	 *(±)-trans*-*N*-methyl-4-phenyl-*N*-[3-(pyridin-3-yl)phenyl]pyrrolidine-3-carboxamide

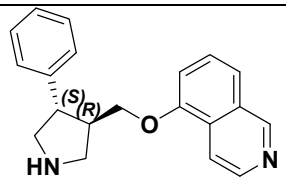
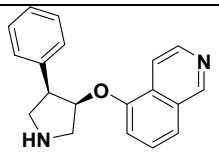
Compound No.	Structure
I-48	 2HCl (±)-trans *(±)-trans*- (4-phenylpyrrolidin-3-yl)[3-(pyridin-3-yl)azetidin-1-yl]methanone dihydrochloride
I-49	 2HCl (±)-trans *(±)-trans*- (4-phenylpyrrolidin-3-yl)[3-(pyridin-3-yl)azetidin-1-yl]methanone dihydrochloride
I-50	 *2HCl *Trans-Rac* *(±)-trans-N*-[3-(pyridin-3-yl)phenyl]-4-(tetrahydro-2*H*-pyran-4-yl)pyrrolidine-3-carboxamide dihydrochloride
I-51	 4-phenyl-*N*-[3-(pyridin-3-yl)phenyl]-1*H*-pyrrole-3-carboxamide

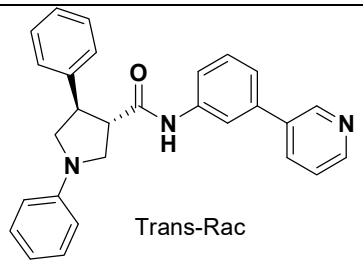
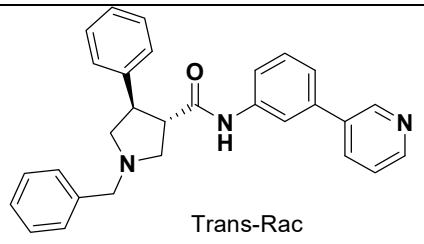
Compound No.	Structure
I-52	 2HCl (±)-trans *(±)-trans-N*-(3-phenoxyphenyl)-4-phenylpyrrolidine-3-carboxamide dihydrochloride
I-53	 3HCl (±)-trans *(±)-trans*-4-phenyl-*N*-[3-(pyrimidin-5-yl)phenyl]pyrrolidine-3-carboxamide triihydrochloride
I-54	 (±)-trans *(±)-trans*-4-phenyl-*N*-[3-(pyridin-3-yl)phenyl]-1-(tetrahydro-2*H*-pyran-4-yl)pyrrolidine-3-carboxamide
I-55	 (±)-trans *(±)-trans*-1-acetyl-4-phenyl-*N*-[3-(pyridin-3-yl)phenyl]pyrrolidine-3-carboxamide

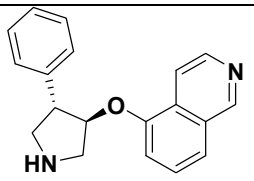
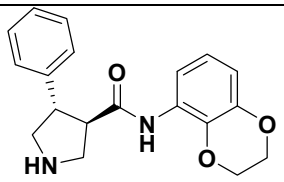
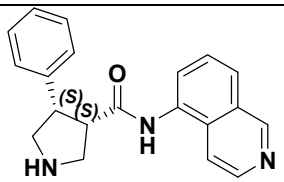
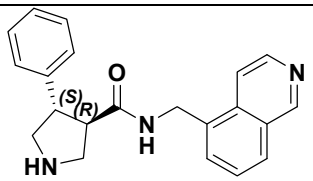
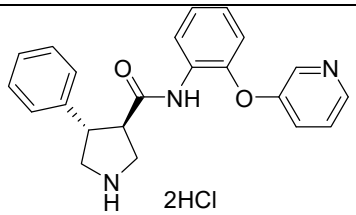
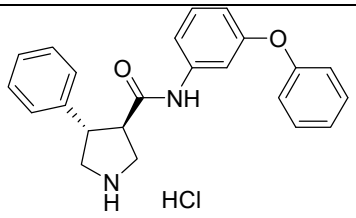
Compound No.	Structure
I-56	 (3*S*,4*S*)-*N*-(isoquinolin-5-yl)-4-(thiophen-2-yl)pyrrolidine-3-carboxamide
I-57	 *2HCl (3*R*,4*S*)-*N*-(isoquinolin-5-yl)-*N*-methyl-4-phenylpyrrolidine-3-carboxamide dihydrochloride

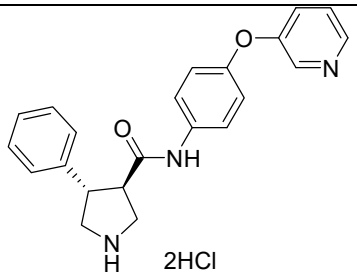
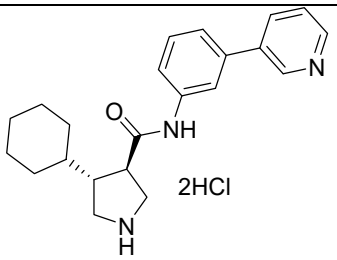
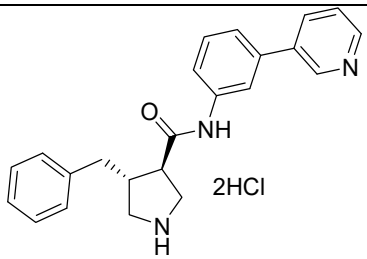
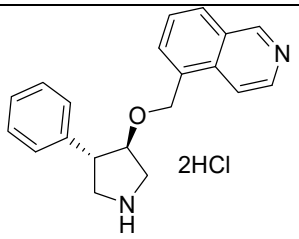
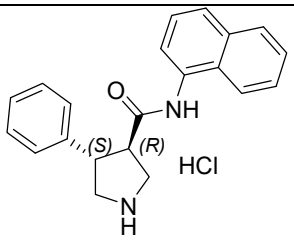
Compound No.	Structure
I-58	 *2HCl (3*R*,4*R*)-*N*-(isoquinolin-5-yl)-4-(1,3-thiazol-2-yl)pyrrolidine-3-carboxamide dihydrochloride
I-59	 *2HCl (3S,4*S*)-*N*-(isoquinolin-5-yl)-4-(1,3-thiazol-2-yl)pyrrolidine-3-carboxamide dihydrochloride

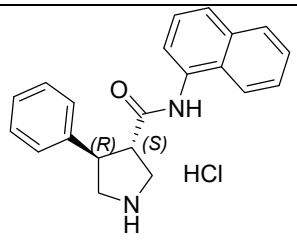
Claim 71. A compound, or a pharmaceutically acceptable salt or tautomer thereof, selected from the group consisting of

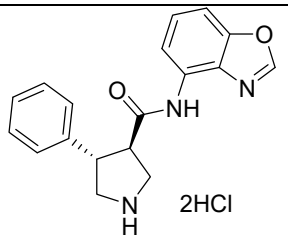
Compound No.	Structure
I-60	 *2HCl
I-61	 *2HCl Cis racemate

Compound No.	Structure
I-62	 Trans-Rac
I-63	 Trans-Rac

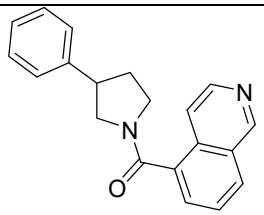
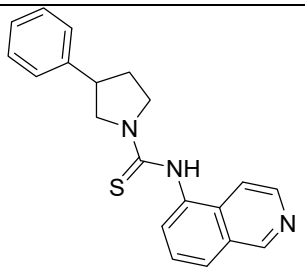
Compound No.	Structure
I-64	 *2HCl Trans-Rac
I-65	 *HCl Trans-Rac
I-66	 *2HCl
I-67	 *2HCl
I-68	 (±)-trans
I-69	 (±)-trans

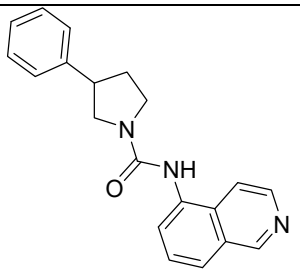
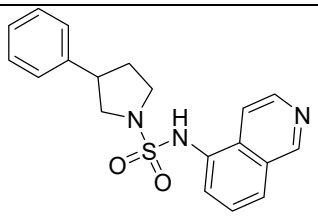
Compound No.	Structure
I-70	 (±)-trans
I-71	 (±)-trans
I-72	 (±)-trans
I-73	 (±)-trans
I-74	

Compound No.	Structure
I-75	

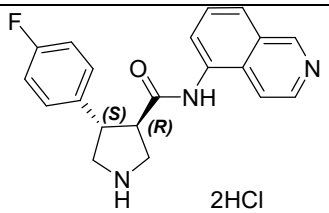
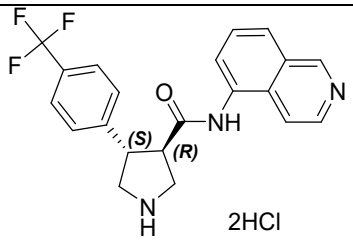
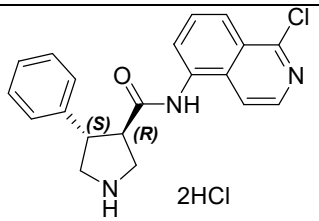
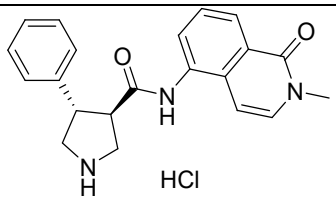
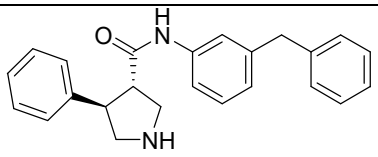
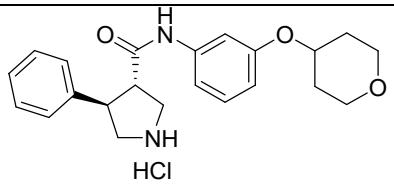
Compound No.	Structure
I-76	

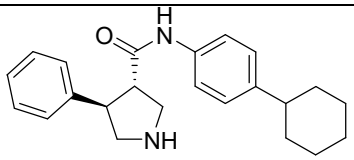
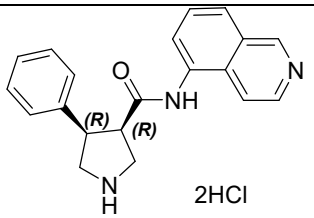
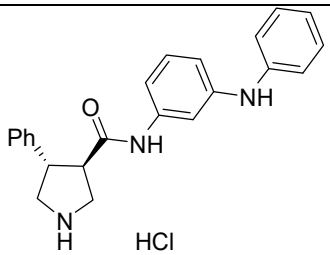
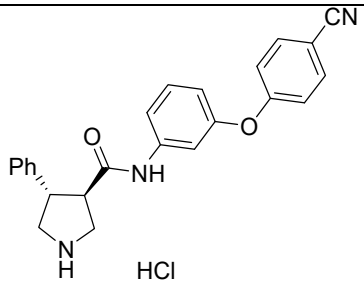
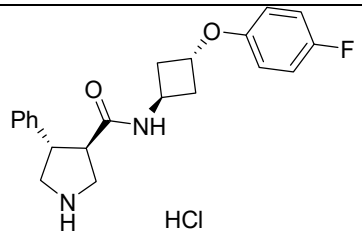
Claim 72. A compound, or a pharmaceutically acceptable salt or tautomer thereof, selected from the group consisting of

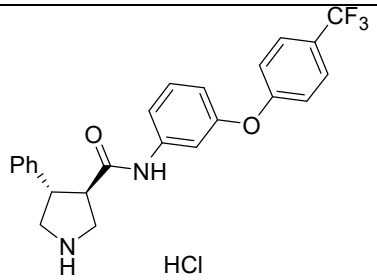
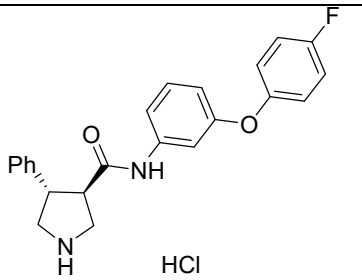
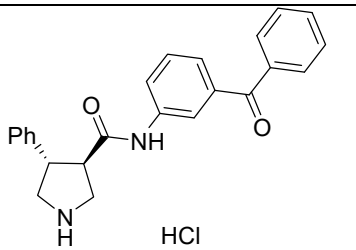
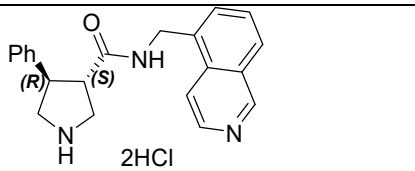
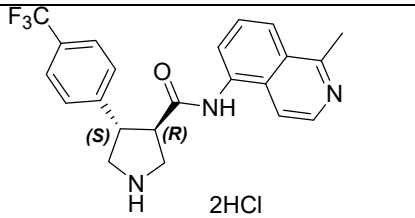
Compound No.	Structure
I-77	 (±)
I-78	 (±)

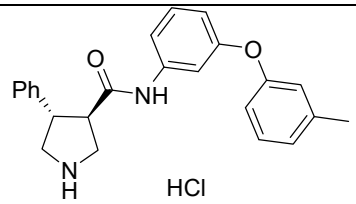
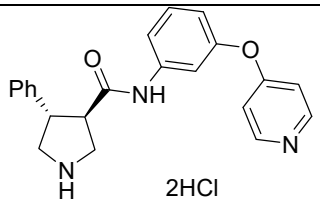
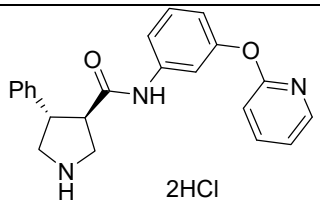
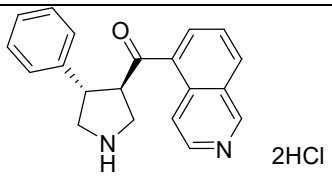
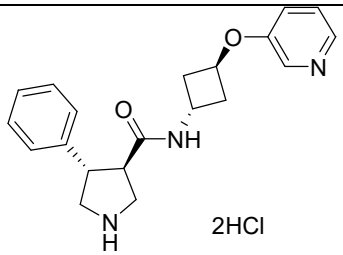
Compound No.	Structure
I-79	 (±)
I-80	 (±)

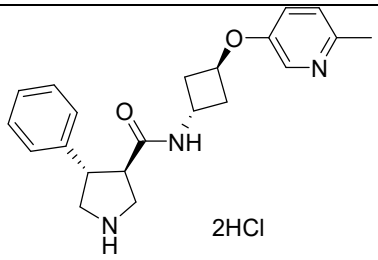
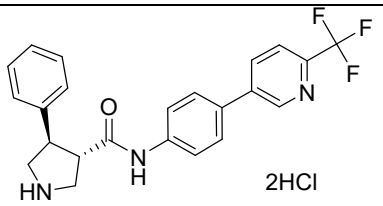
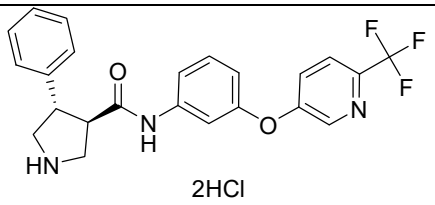
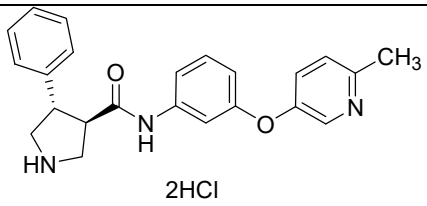
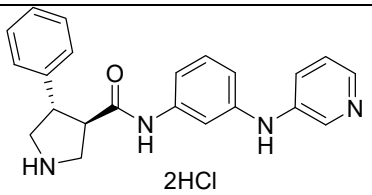
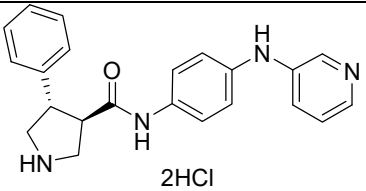
Claim 73. A compound, or a pharmaceutically acceptable salt or tautomer thereof, selected from the group consisting of

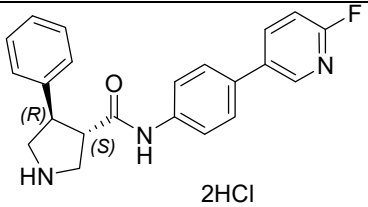
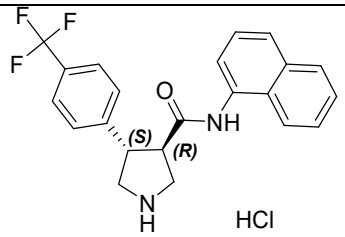
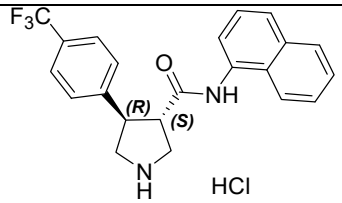
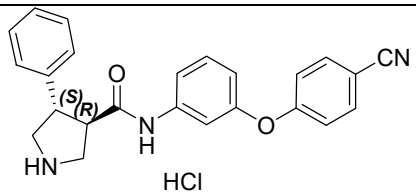
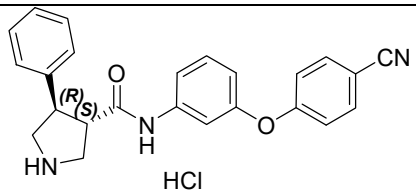
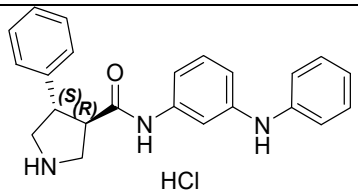
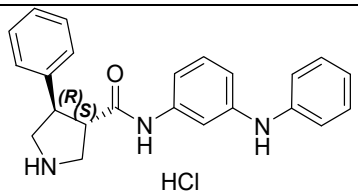
Compound No.	Structure
I-81	 2HCl
I-82	 2HCl
I-83	 2HCl
I-84	 HCl
I-85	 HCl (±)-trans
I-86	 HCl (±)-trans

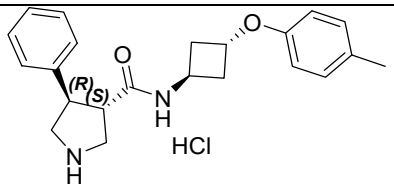
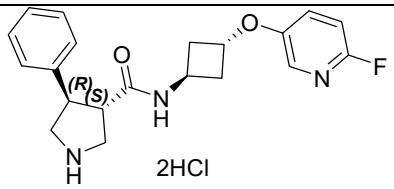
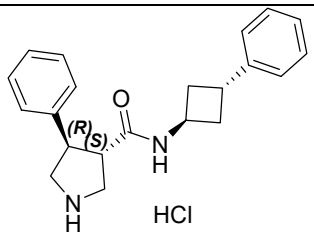
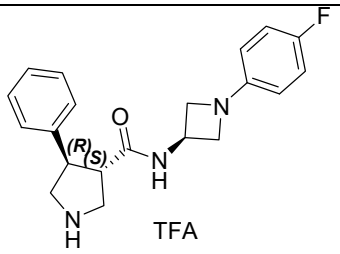
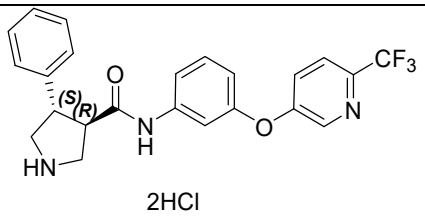
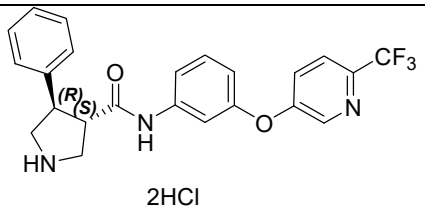
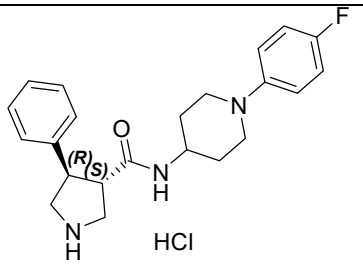
Compound No.	Structure
I-87	 HCl
I-88	 2HCl
I-89	 HCl (±)-trans
I-90	 HCl (±)-trans
I-91	 HCl (±)-trans

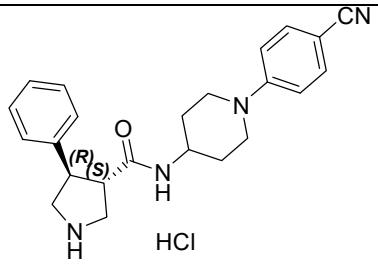
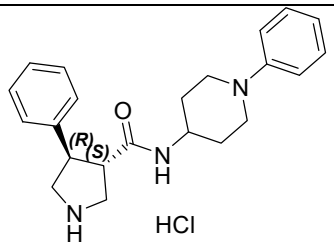
Compound No.	Structure
I-92	 (±)-trans
I-93	 (±)-trans
I-94	 (±)-trans
I-95	
I-96	

Compound No.	Structure
I-97	 (±)-trans
I-98	 (±)-trans
I-99	 (±)-trans
I-100	 (±)-trans
I-101	 (±)-trans

Compound No.	Structure
I-102	 2HCl (±)-trans
I-103	 2HCl
I-104	 2HCl (±)-trans
I-105	 2HCl (±)-trans
I-106	 2HCl (±)-trans
I-107	 2HCl

Compound No.	Structure
	(±)-trans
I-108	 2HCl
I-109	 HCl
I-110	 HCl
I-111	 HCl
I-112	 HCl
I-113	 HCl
I-114	 HCl

Compound No.	Structure
I-115	
I-116	
I-117	
I-118	
I-119	
I-120	
I-121	

Compound No.	Structure
I-122	
I-123	

Claim 74. A pharmaceutical composition, comprising the compound of any one of claims 1 to 73, or a pharmaceutically acceptable salt or tautomer thereof, and a pharmaceutically acceptable excipient.

Claim 75. A method of modulating activity of NR2F6 by exposure of NR2F6 to an effective amount of a compound of any one of claims 1-73, or a pharmaceutically acceptable salt or tautomer thereof, or the pharmaceutical composition of claim 74.

Claim 76. The method of claim 75, wherein said modulation comprises of augmentation of NR2F6 activity.

Claim 77. The method of claim 75, wherein said modulation comprise of inhibition of NR2F6 activity.

Claim 78. ~~A~~Use of the compound of any one of claims 1-73, or a pharmaceutically acceptable salt or tautomer thereof, or the pharmaceutical composition of claim 74~~76~~ in the manufacture of a medicament for treating or reducing the effect of a disease or disorder associated with NR2F6 modulation in a subject, wherein an effective amount of the compound, pharmaceutically acceptable salt, tautomer thereof or the pharmaceutical composition is to be administered to the subject.

Claim 79. The ~~compound~~use of claim 78, wherein the disease or disorder comprises an augmented autoimmune response.

Claim 80. The ~~compound~~use according to claim 79, wherein the augmented autoimmune response is selected from the group consisting of rheumatoid arthritis, systemic lupus erythematosiss (lupus), inflammatory bowel disease, multiple sclerosis, type-1 diabetes mellitus, Guillian-Barre syndrome, chronic inflammatory demyelinating polyneuropathy, psoriasis/psoriatic arthritis, Grave's disease, Hashimoto's thyroiditis, myasthenia gravis, and vasculitis.

Claim 81. The ~~compound~~use of claim 78, wherein the disorder is cancer.

Claim 82. The ~~compound~~use according to claim 81, wherein the cancer is a solid tumor selected from the group consisting of adenocarcinoma of the lung, bile duct cancer, bladder

cancer; bone cancer, brain tumor, glioma, anaplastic oligodendroglioma, adult glioblastoma multiforme, adult anaplastic astrocytoma; benign prostate hyperplasia bronchoalveolar carcinoma, breast cancer, including metastatic breast cancer; cervical cancer, cholangiocarcinoma, colorectal cancer, esophageal cancer, gastric cancer, head and neck cancer, squamous cell carcinoma of the head and neck, gallbladder cancer hepatocellular cancer, kidney cancer, liver cancer, lung cancer, melanoma; neuroendocrine cancer, metastatic neuroendocrine tumor, non-small cell lung cancer (NSCLC), small cell lung cancer, ovarian cancer, primary peritoneal cancer, pancreatic cancer, prostate cancer, including androgen-dependent and androgen-independent prostate cancer, colorectal carcinoma, renal cancer, metastatic renal cell carcinoma, soft tissue sarcoma, urinary bladder cancer, and uterine cancer.

Claim 83. The ~~compound~~use of claim 78, wherein the disorder is a haematological malignancy.

Claim 84. The ~~compound~~use of claim 83, wherein the hematologic malignancy is selected from the group consisting of acute myeloid leukemia, chronic myelogenous leukemia (CML), accelerated CML, CML blast phase (CML-BP), acute lymphoblastic leukemia, chronic lymphocytic leukemia (CLL), Hodgkin's disease, non-Hodgkin's lymphoma, follicular lymphoma, mantle cell lymphoma, B-cell lymphoma, T-cell lymphoma, multiple myeloma, Waldenstrom's macroglobulinemia, myelodysplastic syndromes (MDS), refractory anemia (RA), RA with ringed sideroblasts, RA with excess blasts (RAEB), RAEB in transformation, and a myeloproliferative syndrome.

Claim 85. ~~A~~Use of the compound of any one of claims 1-73, or a pharmaceutically acceptable salt or tautomer thereof, or the pharmaceutical composition of claim 74 in the manufacture of a medicament for treating or reducing the effect of a gastrointestinal disease or disorder in a subject, wherein an effective amount of the compound, pharmaceutically acceptable salt, tautomer thereof or the pharmaceutical composition is to be administered to the subject.

Claim 86. The ~~compound~~use of claim 85, wherein the gastrointestinal disorder is IBD, Crohn’s disease, or colitis.

Claim 87. ~~A~~Use of the compound of any one of claims 1-73, or a pharmaceutically acceptable salt or tautomer thereof, or the pharmaceutical composition of claim 74 in the manufacture of a medicament for treating a condition associated with hepatic steatosis in a subject, wherein an effective amount of the compound, pharmaceutically acceptable salt, tautomer thereof or the pharmaceutical composition is to be administered to the subject.

Claim 88. The ~~compound~~use of claim 87, wherein the condition associated with hepatic steatosis is non-alcoholic fatty liver disease (NAFLD) or non-alcoholic steatohepatitis (NASH).

Claim 89. A compound of any one of claims 1-73, or a pharmaceutically acceptable salt or tautomer thereof, or the pharmaceutical composition of claim 74 for use in modulating activity of NR2F6.

Claim 90. A compound of any one of claims 1-73, or a pharmaceutically acceptable salt or tautomer thereof, or the pharmaceutical composition of claim 74 for use in treating or reducing the effect of a disease or disorder associated with NR2F6 modulation.

~~Claim 91. Use of a compound of any one of claims 1-73, or a pharmaceutically acceptable salt or tautomer thereof, or the pharmaceutical composition of claim 74, for modulating activity of NR2F6.~~

~~Claim 92. Use of a compound of any one of claims 1-73, or a pharmaceutically acceptable salt or tautomer thereof, or the pharmaceutical composition of claim 74, for treating or reducing the effect of a disease or disorder associated with NR2F6 modulation.~~

~~Claim 93. Use of a compound of any one of claims 1-73, or a pharmaceutically acceptable salt or tautomer thereof, or the pharmaceutical composition of claim 74, in the manufacture of a medicament for modulating activity of NR2F6.~~

~~Claim 94. Use of a compound of any one of claims 1-73, or a pharmaceutically acceptable salt or tautomer thereof, or the pharmaceutical composition of claim 74, in the manufacture of a medicament for treating or reducing the effect of a disease or disorder associated with NR2F6 modulation.~~

Claim 91. A compound of any one of claims 1-73, or a pharmaceutically acceptable salt or tautomer thereof, or the pharmaceutical composition of claim 74 for use in therapy.