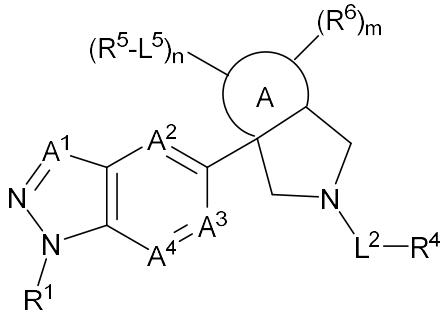
WHAT IS CLAIMED IS:

Claim 1. A compound of Formula I:



(I)

or a pharmaceutically acceptable salt thereof, wherein

R^1 is heterocycloalkyl having 3 to 12 ring members and 1 to 4 heteroatoms each N, O or S, phenyl or heteroaryl having 5 to 10 ring members and 1 to 5 heteroatoms each N, O or S, each independently substituted with 0 to 5 R^{1a} groups;

each R^{1a} is independently C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxyalkyl, C_{1-6} hydroxyalkyl, halogen, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, -OH, oxo, -CN, -C(O)N(R^{1b})(R^{1c}), C_{3-10} cycloalkyl, or heterocycloalkyl having 3 to 12 ring members and 1 to 4 heteroatoms each N, O or S;

each R^{1b} and R^{1c} is independently hydrogen, C_{1-6} alkyl or a 3 to 8 membered heterocycloalkyl having 1 to 3 heteroatoms each independently N, O or S;

A^1, A^2, A^3 and A^4 are each independently =CR^2- or =N-;

each R^2 is independently hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{2-6} alkoxyalkyl, halogen, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, hydroxy, C_{1-6} hydroxyalkyl, or -CN;

Ring A is a C_{3-6} cycloalkyl;

L^2 is absent, -C(O)-, -C(O)O-, -C(O)N(R^3)-, -S(O)$_2$- or -S(O)$_2$N(R^3)-;

R^3 is hydrogen or C_{1-6} alkyl;

R^4 is C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} alkoxyalkyl, -$(CH_2CH_2O)_{2-6}CH_3$, C_{1-6} hydroxyalkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{1-6} alkyl-C_{3-8} cycloalkyl, heterocycloalkyl, C_{1-6} alkyl-heterocycloalkyl, C_{6-12} aryl, C_{1-6} alkyl-C_{6-12} aryl, heteroaryl, or C_{1-6} alkyl-heteroaryl, wherein each heterocycloalkyl independently has 3 to 12 ring members and 1 to 3 heteroatoms each independently N, O or S, wherein each heteroaryl independently has 5 to 10 ring members and 1 to 4 heteroatoms each independently N, O or S, and

wherein each cycloalkyl, heterocycloalkyl, aryl and heteroaryl is independently substituted with 0 to 5 R^{4a} groups;

alternatively, R^3 and R^4 are combined with the atoms to which they are attached to form a heterocycloalkyl having 3 to 12 ring members and 1 to 3 additional heteroatoms each independently N, O or S, wherein the heterocycloalkyl is substituted with 0, 1 or 2 C_{1-6} alkyl groups;

each R^{4a} is independently C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{2-6} alkoxyalkyl, C_{1-6} hydroxyalkyl, halogen, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, -CN, -OH, oxo, $-C(O)R^{4b}$, $-C(O)OR^{4b}$, $-OC(O)R^{4b}$, $-OC(O)OR^{4b}$, $-C(O)N(R^{4b})(R^{4c})$, $-N(R^{4b})C(O)R^{4c}$, $-OC(O)N(R^{4b})(R^{4c})$, $-N(R^{4b})C(O)OR^{4c}$, $-S(O)_2R^{4b}$, $-S(O)_2N(R^{4b})(R^{4c})$, $-N(R^{4b})S(O)_2R^{4c}$, C_{3-8} cycloalkyl, C_{1-6} alkyl-C_{3-8} cycloalkyl, heterocycloalkyl, C_{1-6} alkyl-heterocycloalkyl, C_{6-12} aryl, C_{1-6} alkyl-C_{6-12} aryl, heteroaryl, or C_{1-6} alkyl-heteroaryl, wherein each heterocycloalkyl independently has 3 to 12 ring members and 1 to 3 heteroatoms each independently N, O or S, wherein each heteroaryl independently has 5 to 10 ring members and 1 to 4 heteroatoms each independently N, O or S, and wherein each cycloalkyl, heterocycloalkyl, aryl and heteroaryl is substituted with 0, 1 or 2 C_{1-6} alkyl groups;

each R^{4b} and R^{4c} is hydrogen or C_{1-6} alkyl;

each L^5 is independently absent or C_{1-6} alkylene;

each R^5 is independently C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{2-6} alkoxyalkyl, hydroxy, C_{1-6} hydroxyalkyl, halogen, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, -CN, oxo, $-OR^{5a}$, $-C(O)R^{5a}$, $-C(O)OR^{5a}$, $-OC(O)R^{5a}$, $-C(O)N(R^{5a})(R^{5b})$, $-N(R^{5a})C(O)R^{5b}$, $-OC(O)N(R^{5a})(R^{5b})$, $-N(R^{5a})C(O)OR^{5b}$, $-S(O)_2R^{5a}$, $-S(O)_2N(R^{5a})(R^{5b})$, $-N(R^{5a})S(O)_2R^{5b}$, C_{3-8} cycloalkyl, heterocycloalkyl, C_{6-12} aryl, or heteroaryl, wherein each heterocycloalkyl independently has 3 to 12 ring members and 1 to 3 heteroatoms each independently N, O or S, wherein each heteroaryl independently has 5 to 10 ring members and 1 to 4 heteroatoms each independently N, O or S, and wherein each cycloalkyl, heterocycloalkyl, aryl and heteroaryl is independently substituted with 0 to 4 R^{5c} groups;

each R^{5a} and R^{5b} is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} alkoxyalkyl, hydroxy, C_{1-6} hydroxyalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{3-8} cycloalkyl, C_{1-6} alkyl-C_{3-8} cycloalkyl, heterocycloalkyl, C_{1-6} alkyl-

heterocycloalkyl, C_{6-12} aryl, C_{1-6} alkyl-C_{6-12} aryl, heteroaryl, or C_{1-6} alkyl-heteroaryl, wherein each heterocycloalkyl independently has 3 to 12 ring members and 1 to 3 heteroatoms each independently N, O or S, wherein each heteroaryl independently has 5 to 10 ring members and 1 to 4 heteroatoms each independently N, O or S, and wherein each cycloalkyl, heterocycloalkyl, aryl and heteroaryl is subsituted with 0 to 4 R^{5d} groups;

alternatively, R^{5a} and R^{5b} are combined with the atoms to which they are attached to form a heterocycloalkyl having 3 to 12 ring members and 1 to 3 additional heteroatoms each independently N, O or S, wherein the heterocycloalkyl is substituted with 0, 1 or 2 C_{1-6} alkyl groups;

each R^{5c} is independently C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{2-6} alkoxyalkyl, hydroxy, C_{1-6} hydroxyalkyl, halogen, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, -CN, oxo, -OH, $-C(O)R^{5c1}$, $-C(O)OR^{5c1}$, $-OC(O)R^{5c1}$, $-OC(O)OR^{5c1}$, $-C(O)N(R^{5c1})(R^{5c2})$, $-N(R^{5c1})C(O)R^{5c2}$, $-OC(O)N(R^{5c1})(R^{5c2})$, $-N(R^{5c1})C(O)OR^{5c2}$, $-S(O)_2R^{5c1}$, $-S(O)_2N(R^{5c1})(R^{5c2})$, $-N(R^{5c1})S(O)_2R^{5c2}$, C_{3-8} cycloalkyl, C_{1-6} alkyl-C_{3-8} cycloalkyl, heterocycloalkyl, C_{1-6} alkyl-heterocycloalkyl, C_{6-12} aryl, C_{1-6} alkyl-C_{6-12} aryl, heteroaryl, or C_{1-6} alkyl-heteroaryl, wherein each heterocycloalkyl independently has 3 to 12 ring members and 1 to 3 heteroatoms each independently N, O or S, wherein each heteroaryl independently has 5 to 10 ring members and 1 to 4 heteroatoms each independently N, O or S, and wherein each heterocycloalkyl and heteroaryl is substituted with 0, 1 or 2 C_{1-6} alkyl groups;

each R^{5c1} and R^{5c2} is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} alkoxyalkyl, C_{1-6} hydroxyalkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{1-6} alkyl-C_{3-8} cycloalkyl, heterocycloalkyl, C_{1-6} alkyl-heterocycloalkyl, C_{6-12} aryl, C_{1-6} alkyl-C_{6-12} aryl, heteroaryl, or C_{1-6} alkyl-heteroaryl, wherein each heterocycloalkyl independently has 3 to 12 ring members and 1 to 3 heteroatoms each independently N, O or S, wherein each heteroaryl independently has 5 to 10 ring members and 1 to 4 heteroatoms each independently N, O or S, and wherein each heterocycloalkyl and heteroaryl is substituted with 0, 1 or 2 C_{1-6} alkyl groups;

alternatively, R^{5c1} and R^{5c2} are combined with the atoms to which they are attached to form a heterocycloalkyl having 3 to 12 ring members and 1 to 3 additional

heteroatoms each independently N, O or S, wherein the heterocycloalkyl is substituted with 0, 1 or 2 C_{1-6} alkyl groups;

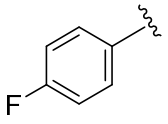
each R^{5d} is independently C_{1-6} alkyl or halogen;

each R^6 is independently C_{1-6} alkoxy, hydroxy, C_{1-6} hydroxyalkyl, halogen, C_{1-6} haloalkyl, or C_{1-6} haloalkoxy;

subscript m is 0, 1, 2, 3, 4 or 5; and

subscript n is 1 or 2.

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



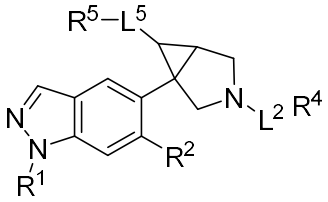
.

Claim 3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein

A^1, A^2 and A^4 are each =CH-; and

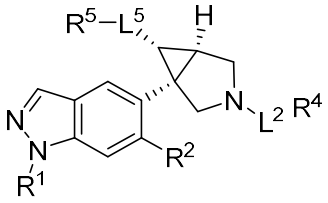
A^3 is =CH- or =C(Me)-.

Claim 4. The compound of any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, having the structure of Formula Ib:



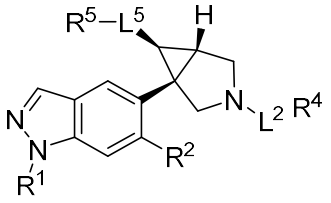
(Ib) .

Claim 5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, having the structure of Formula Ib-1:



(Ib-1) .

Claim 6. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, having the structure of Formula Ib-2:

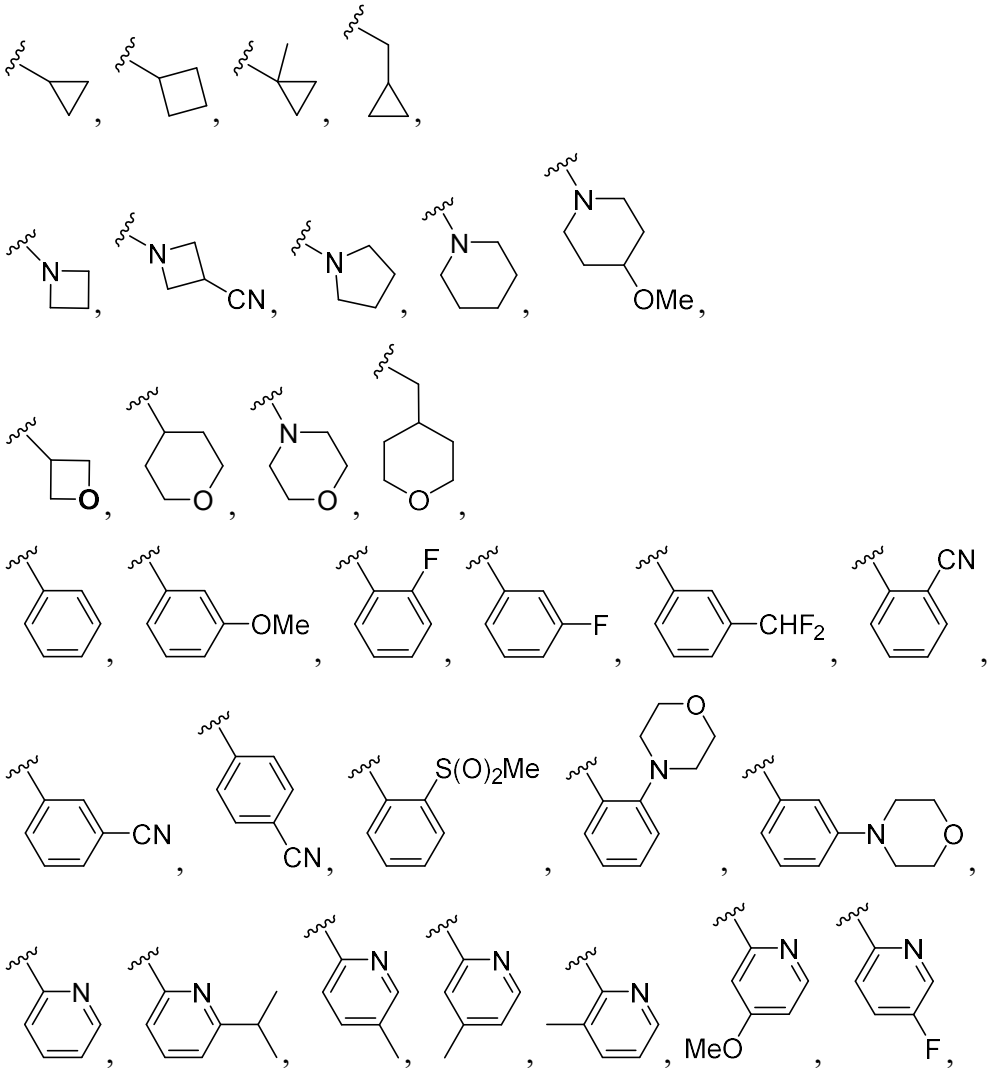


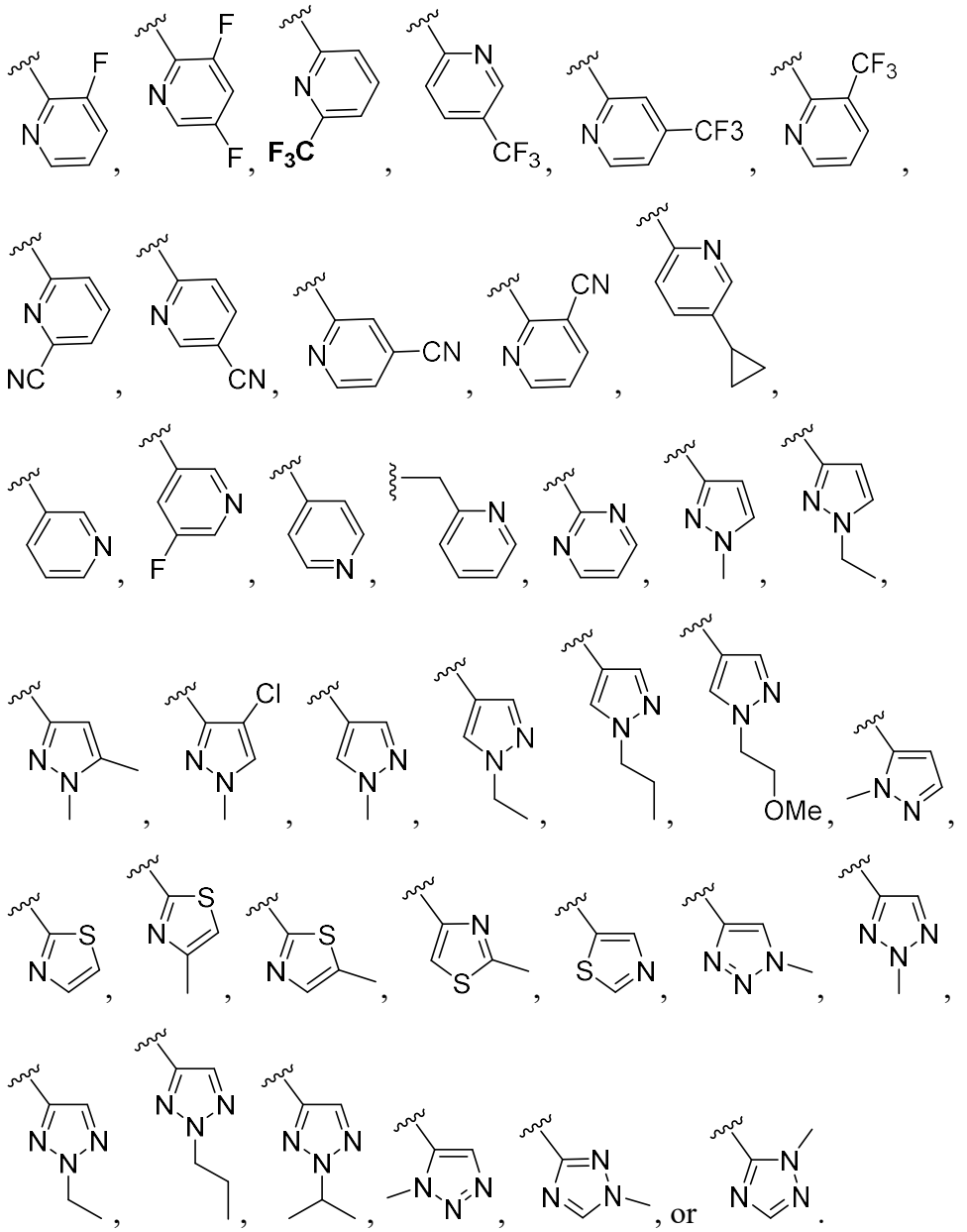
(Ib-2) .

Claim 7. The compound of any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein L^2 is -C(O)-.

Claim 8. The compound of any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, wherein

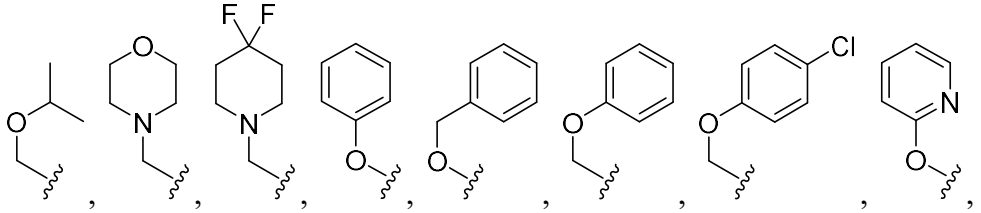
R^4 is methyl, ethyl, iso-propyl, iso-butyl, t-butyl, methoxymethyl, methoxyethyl, -$(CH_2CH_2O)_2CH_3$,

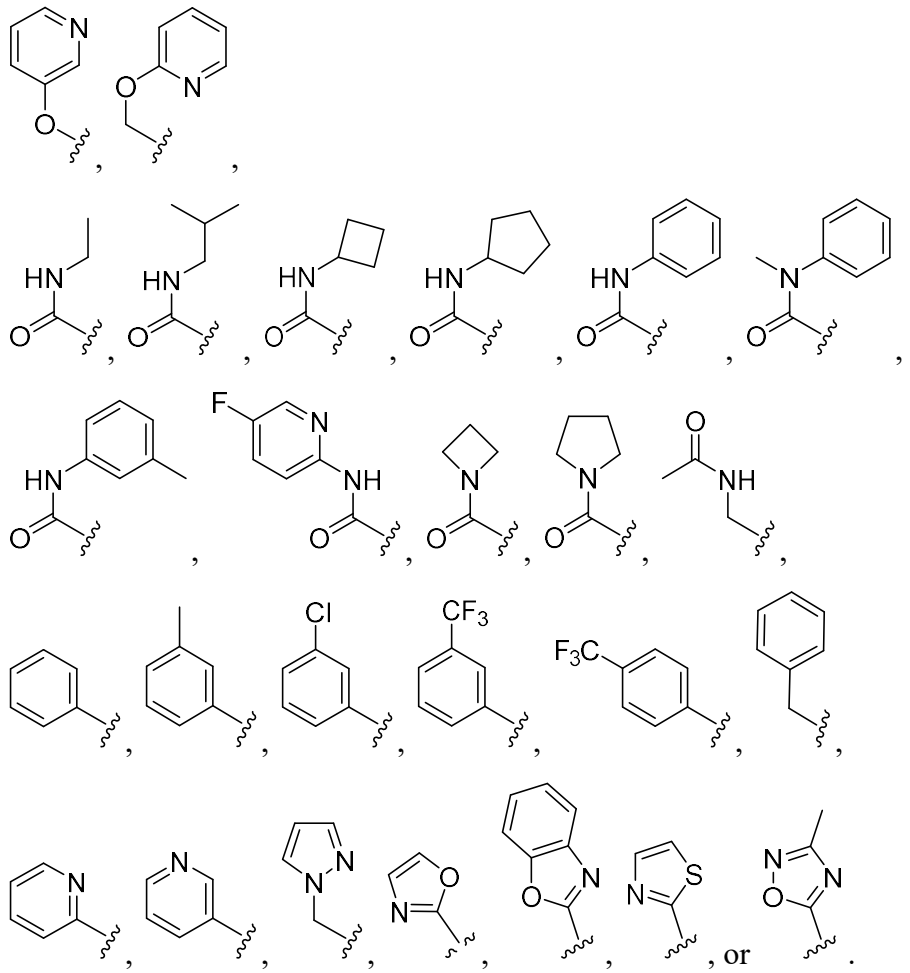




Claim 9. The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, wherein

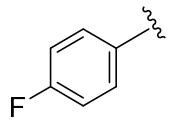
each R^5-L^5- group is methyl, -C≡CCH_3, methoxy, –CH_2OH, oxo,





Claim 10. The compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, wherein

R^1 is



;

A^1, A^2 and A^4 are each =CH-;

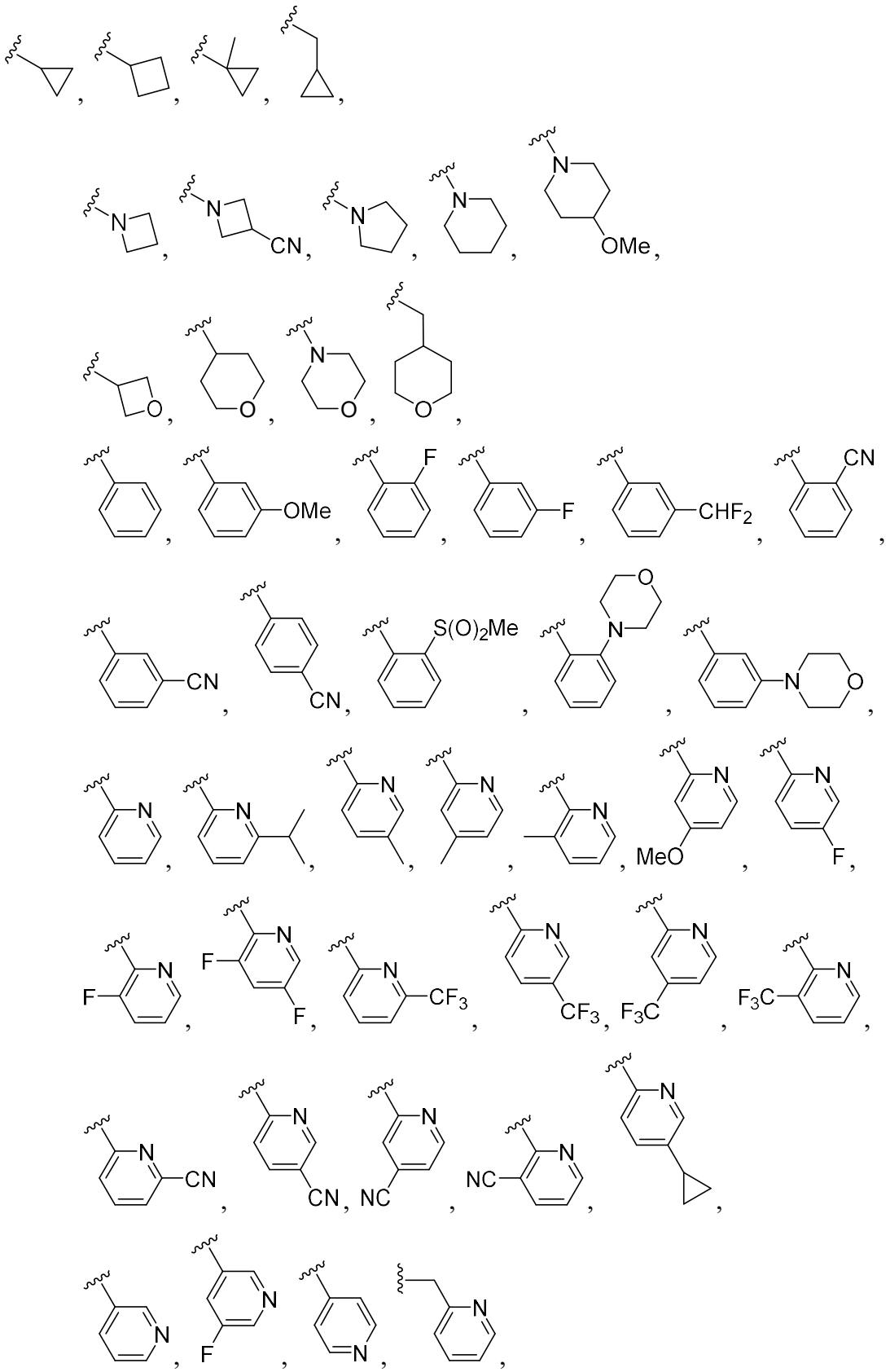
A^3 is =CH- or =C(Me)-;

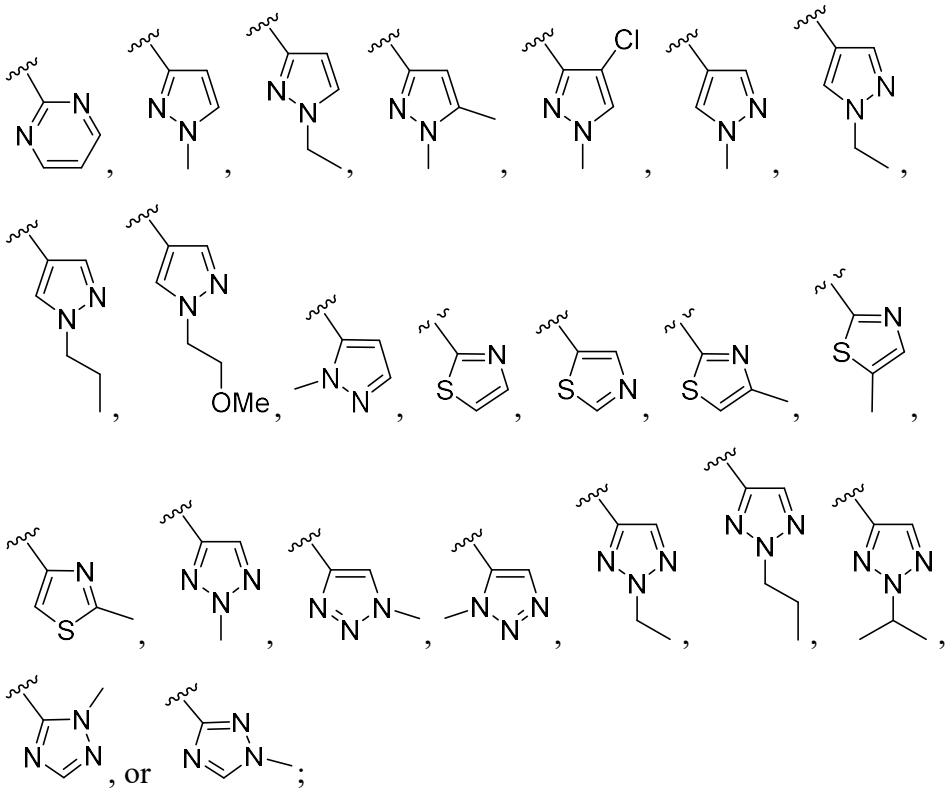
Ring A is a C_3 cycloalkyl or a C_5 cycloalkyl;

L^2 is absent, -C(O)-, -C(O)O-, $-S(O)_2-$ or $-S(O)_2N(R^3)-$;

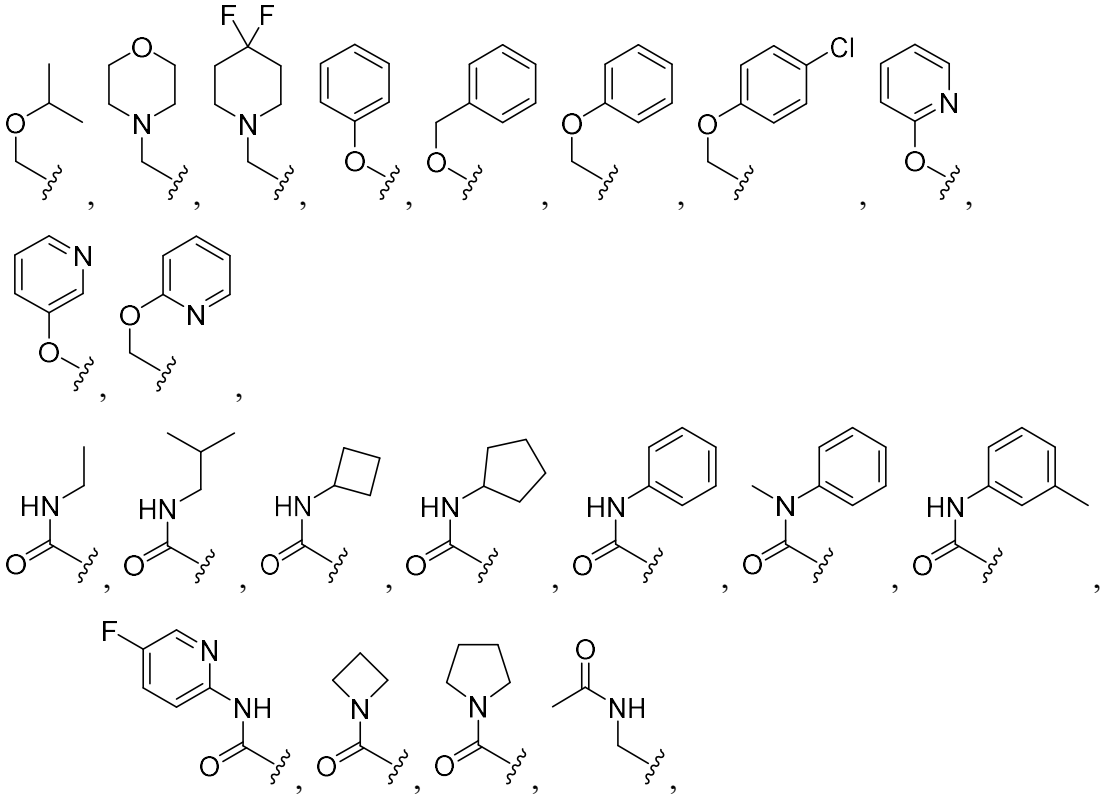
R^3 is hydrogen or methyl;

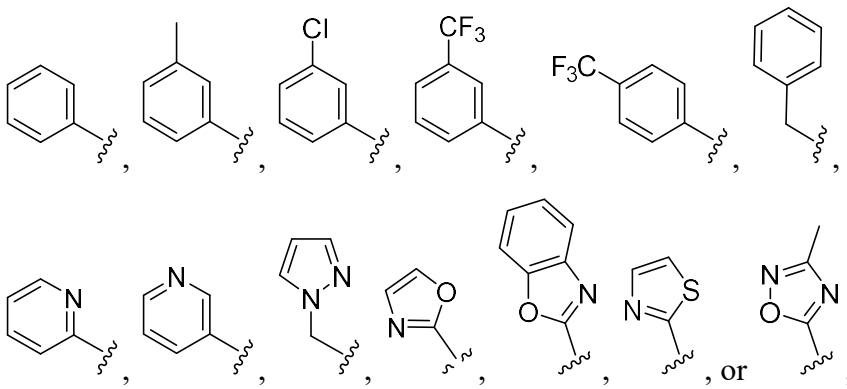
R^4 is methyl, ethyl, iso-propyl, iso-butyl, t-butyl, methoxymethyl, methoxyethyl, $CH_2(CH_2OCH_2)_2H$,





each R^5-L^5- group is methyl, -C≡CCH_3, methoxy, –CH_2OH, oxo,





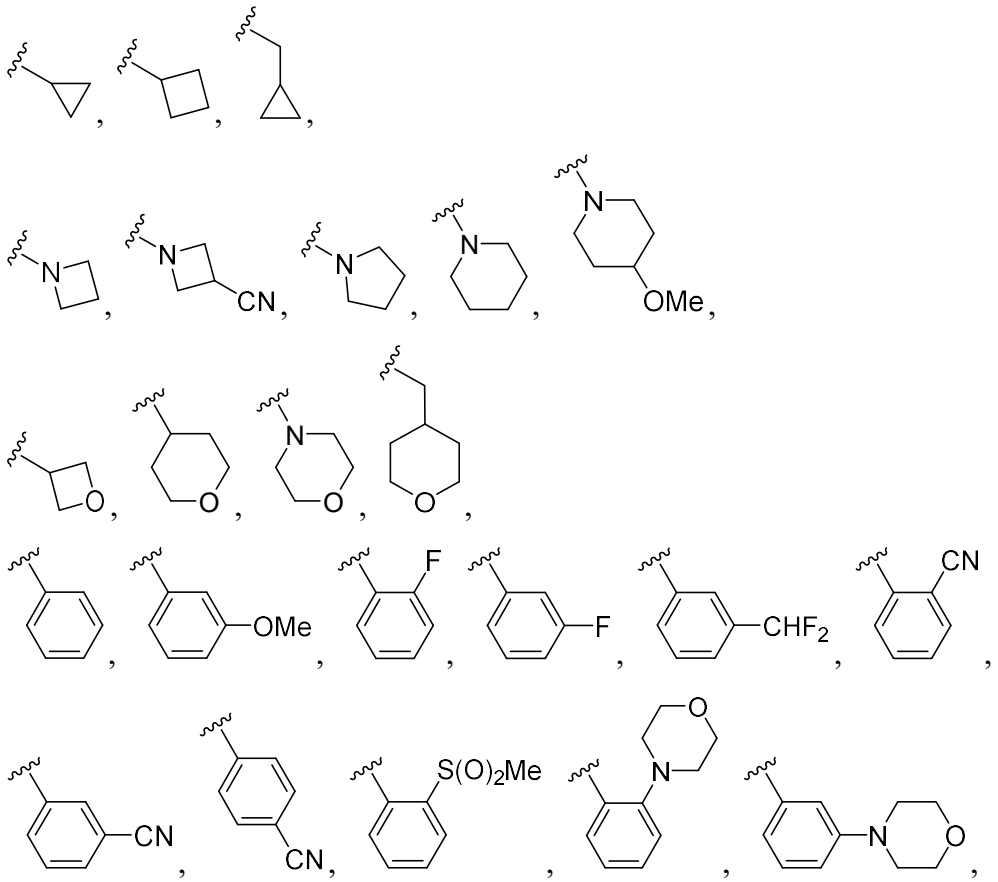
each R^6 is independently –OMe, -OEt, hydroxy, or F;

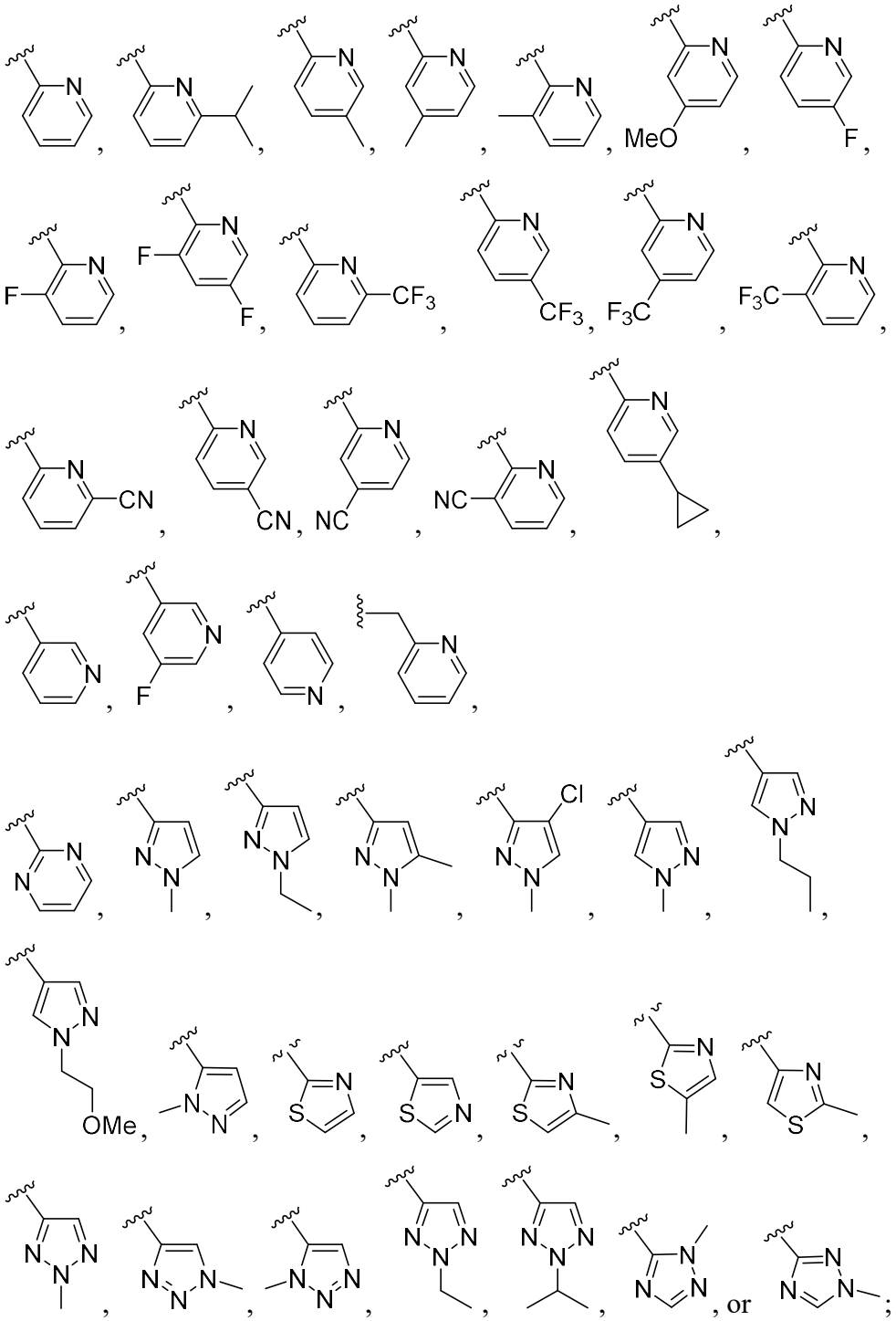
subscript m is 0 or 1; and

subscript n is 1.

Claim 11. The compound of any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, wherein

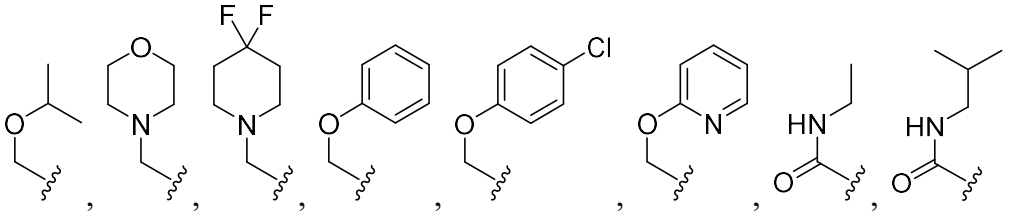
R^4 is methyl, ethyl, iso-propyl, iso-butyl, methoxymethyl, methoxyethyl, $CH_2(CH_2OCH_2)_2H$,

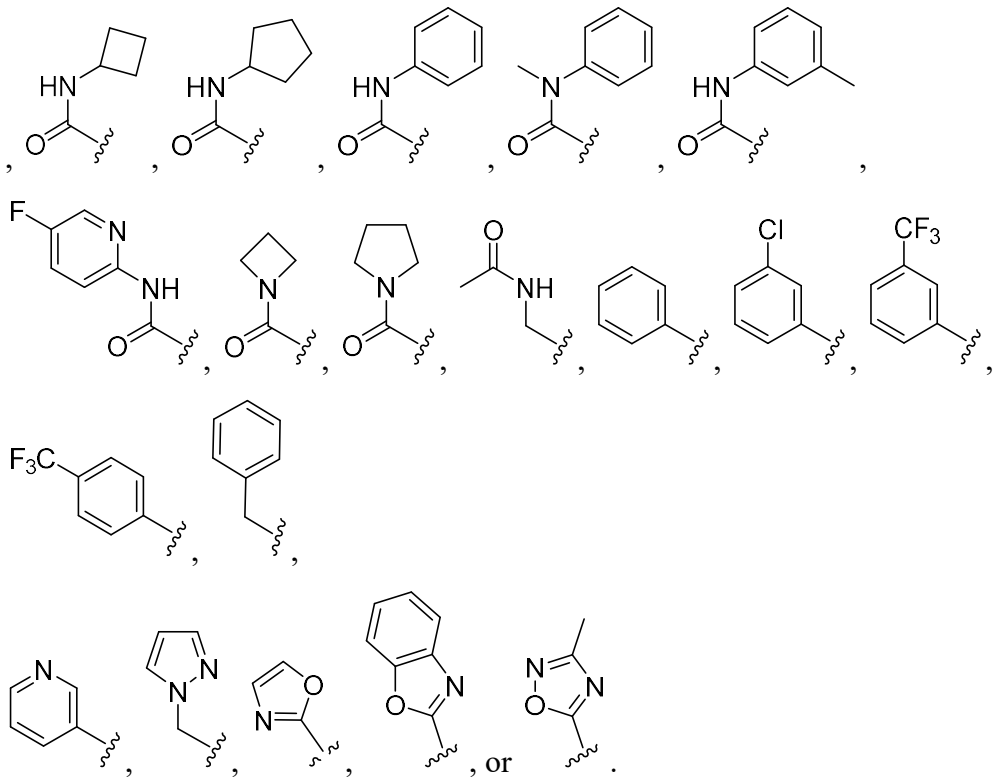




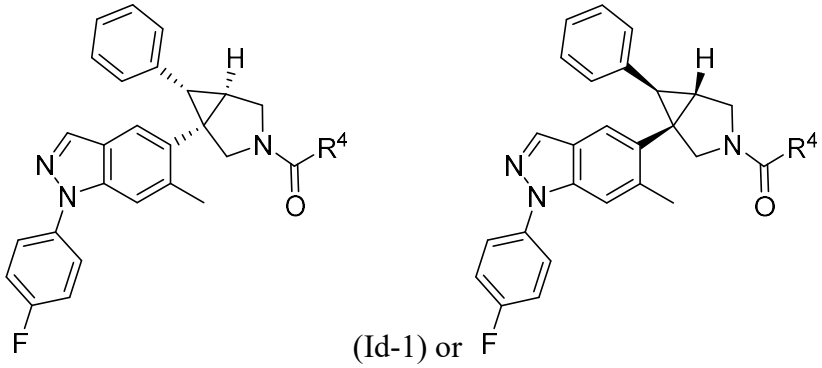
and

each R^5-L^5- group is methyl, $–CH_2OH$,





Claim 12. The compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, having the structure of Formula Id-1 or Id-2:



(Id-1) or (Id-2) .

Claim 13. The compound of any one of claims 1 to 7, 9 or 12 or a pharmaceutically acceptable salt thereof, wherein

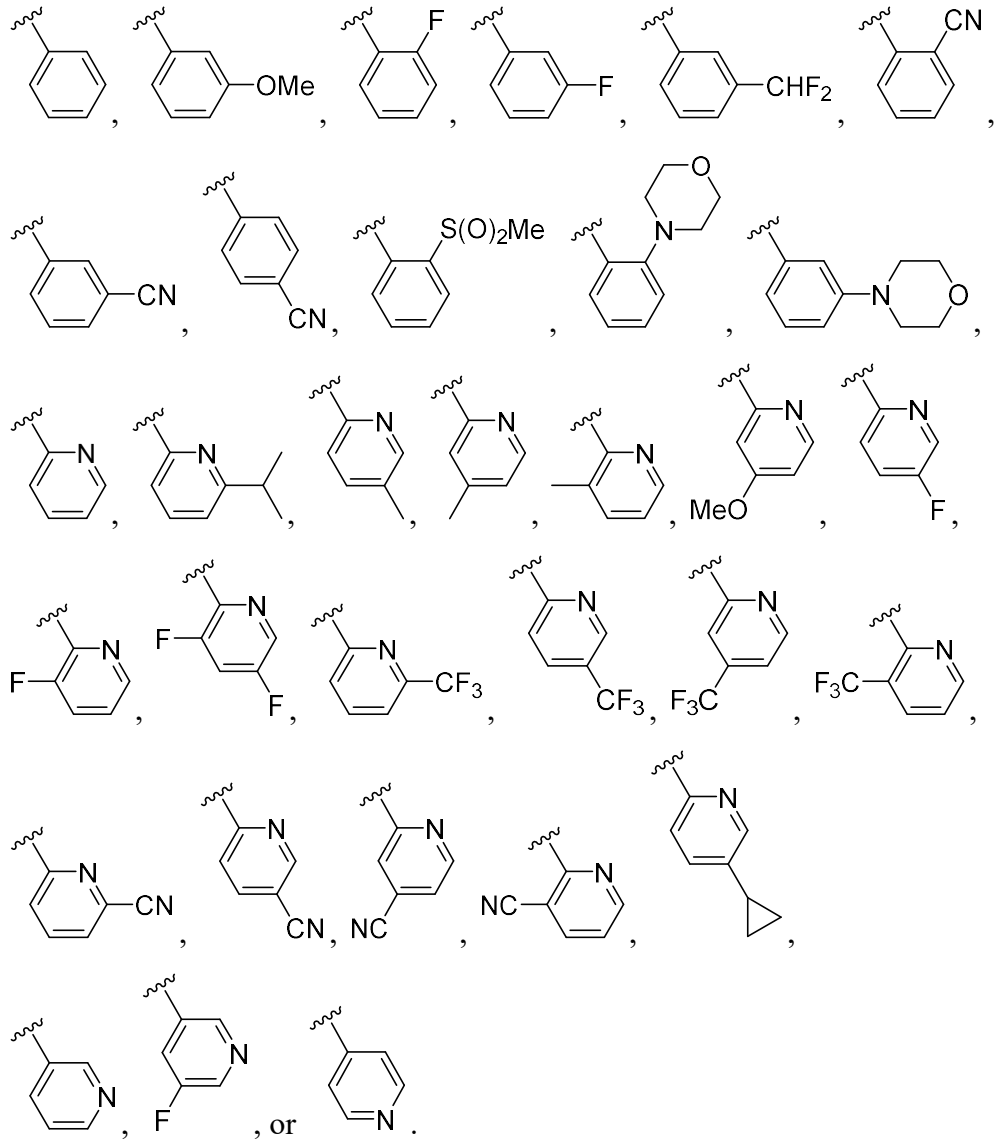
R^4 is C_{6-12} aryl, or heteroaryl having 5 to 6 ring members and 1 to 4 heteroatoms each independently N, O or S, and wherein aryl and heteroaryl are independently substituted with 0 to 3 R^{4a} groups;

each R^{4a} is independently C_{1-3} alkyl, C_{1-3} alkoxy, halogen, C_{1-3} haloalkyl, –CN, -$S(O)_2R^{4b}$, C_{3-6} cycloalkyl, and heterocycloalkyl, wherein each heterocycloalkyl independently has 5 to 6 ring members and 1 to 2 heteroatoms each independently N, O or S; and

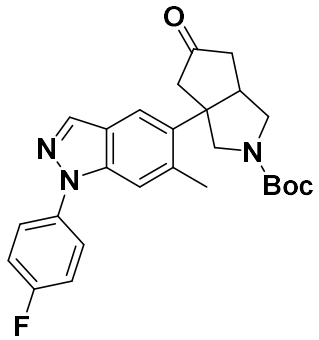
each R^{4b} is C_{1-3} alkyl.

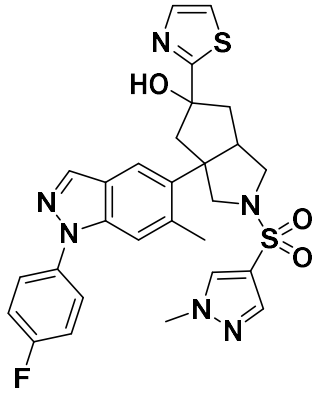
Claim 14. The compound of any one of claims 1 to 13, or a pharmaceutically acceptable salt thereof, wherein

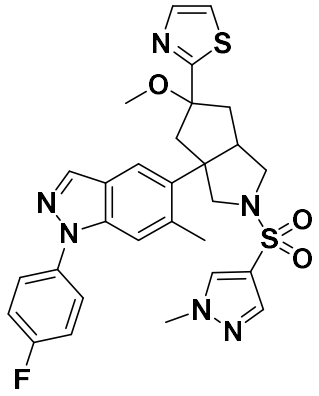
R^4 is

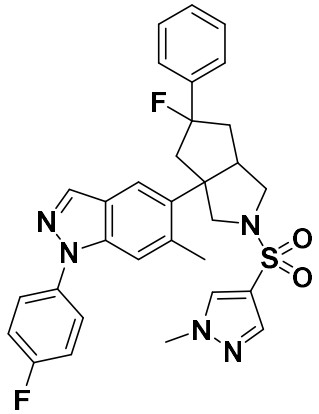


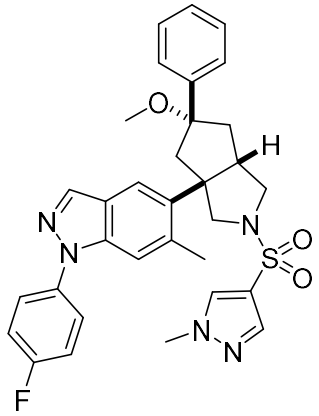
Claim 15. The compound of any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, having the structure of:

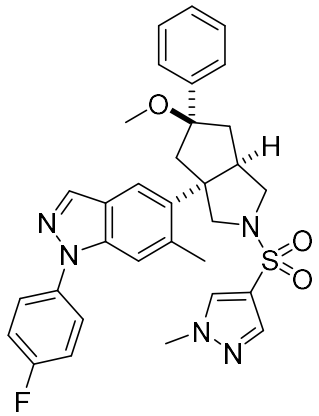

O
N
N
N
Boc
F
;

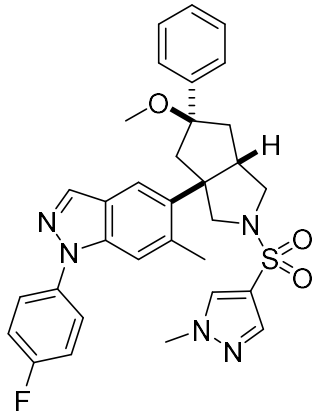

N
S
HO
N
N
N
S
O
O
N
N
F
;

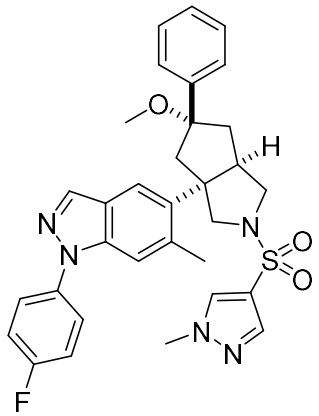

N
S
O
N
N
N
S
O
O
N
N
F
;

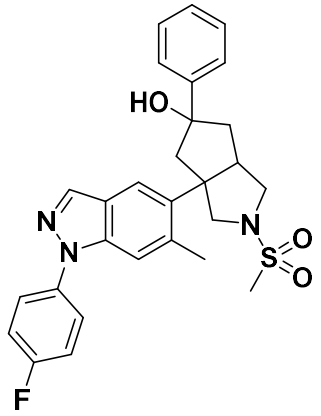

F
N
N
N
S
O
O
N
N
F
;

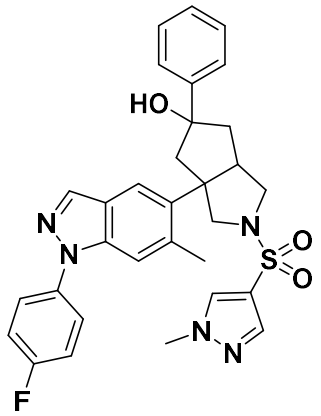

O
H
N
N
S
O
O
N
N
F
;

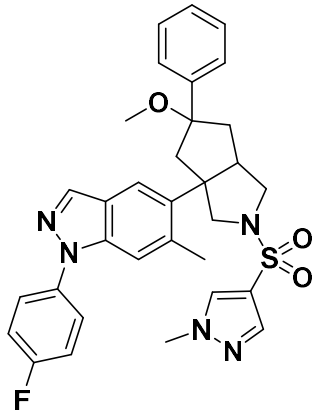

O
H
N
N
S
O
O
N
N
F
;

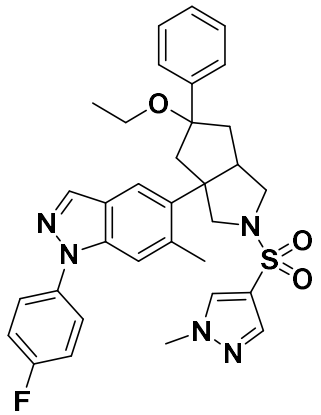

O
H
N
N
S
O
O
N
N
F
;

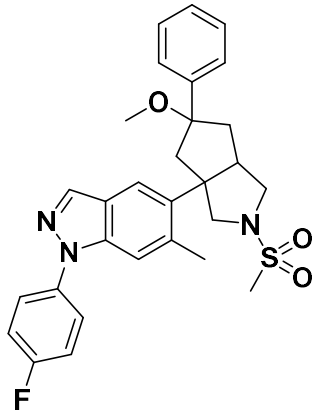

O
H
N
N
S
O
O
N
N
F
;

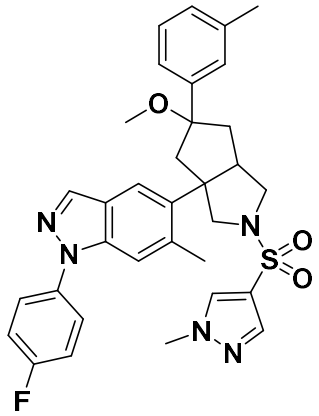

HO
N
N
N
S
O
O
F
;

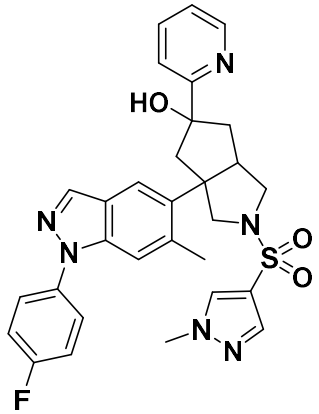

HO
N
N
N
S
O
O
N
N
F
;

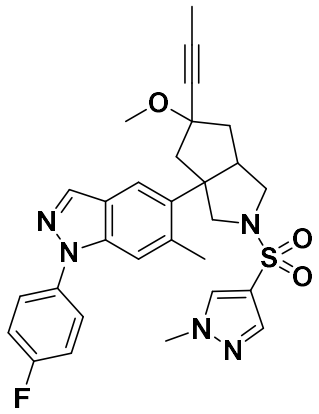

O
N
N
N
S
O
O
N
N
F
;

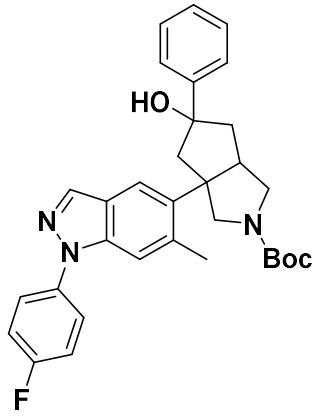

O
N
N
N
S
O
O
N
N
F
;


O
N
N
N
S
O
O
F
;

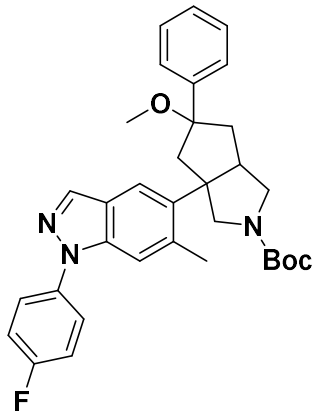

O
N
N
N
S
O
O
N
N
F
;


N
HO
N
N
N
S
O
O
N
N
F
;

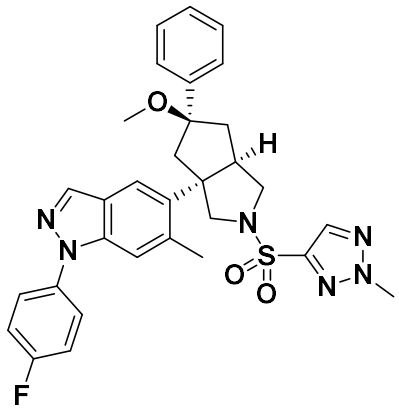

O
N
N
N
S
O
O
N
N
F
;

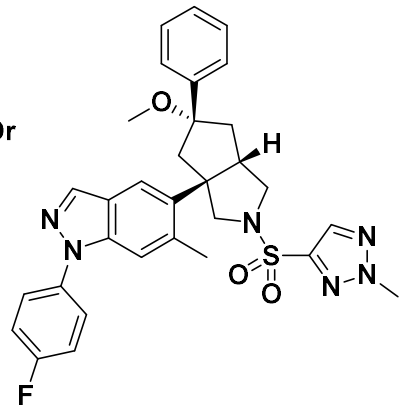


;

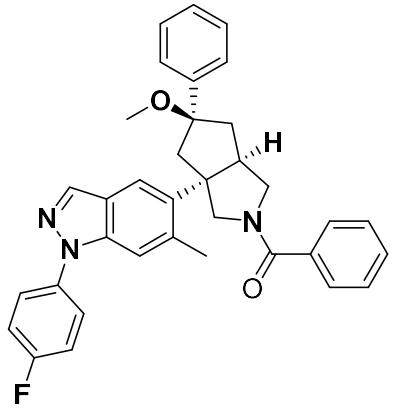


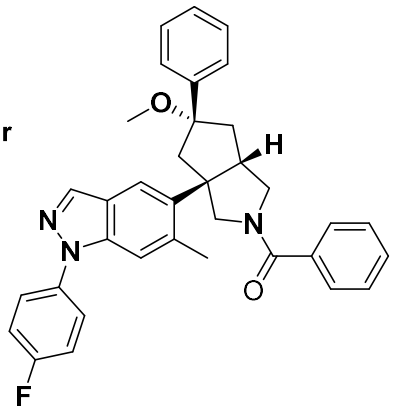
;



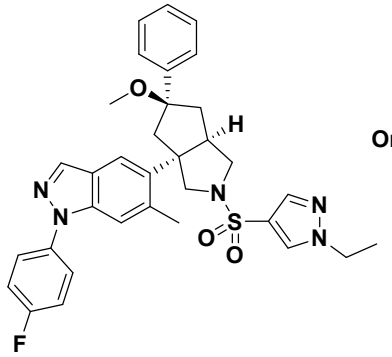
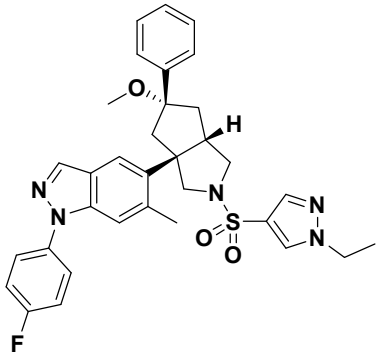
Or


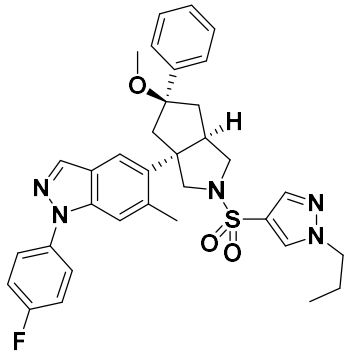
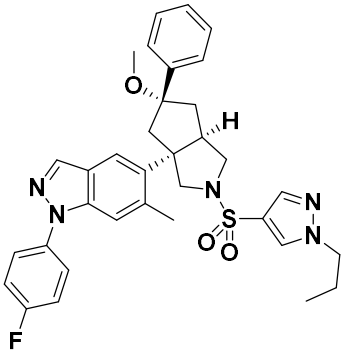
;

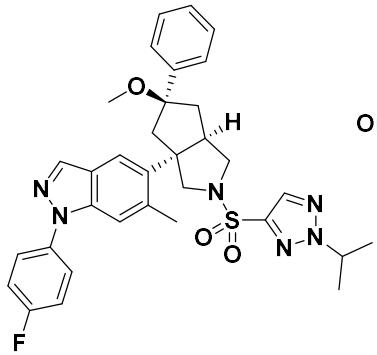
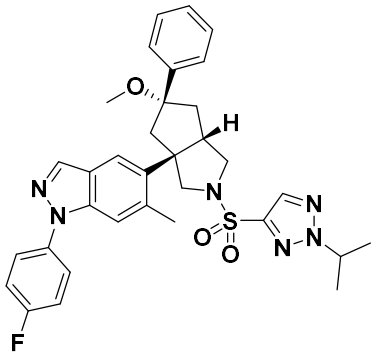


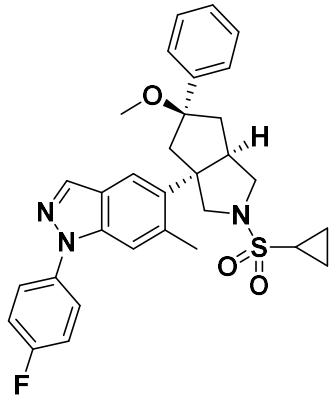
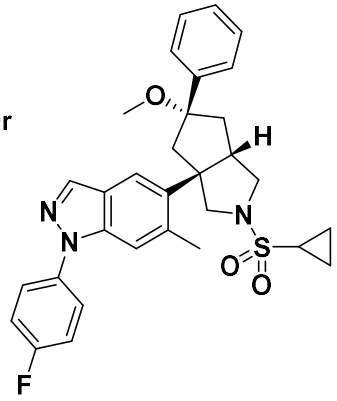
Or


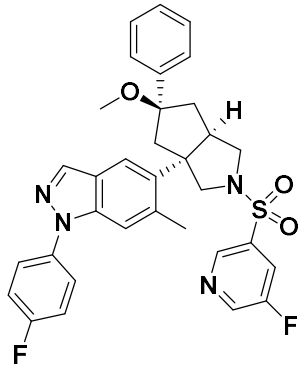
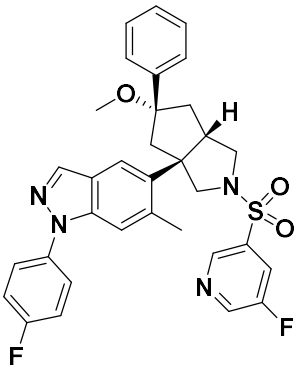
;

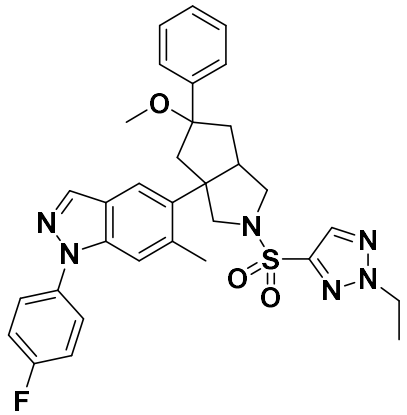

Or

;

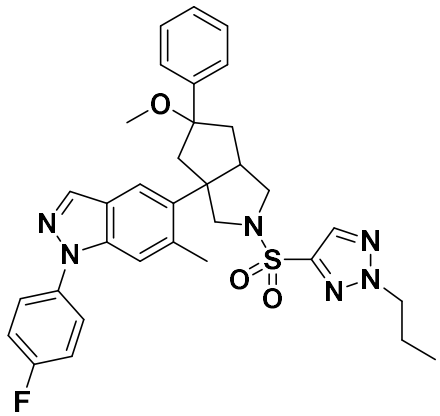

Or

;

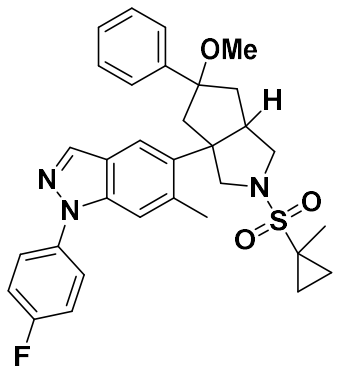

Or

;

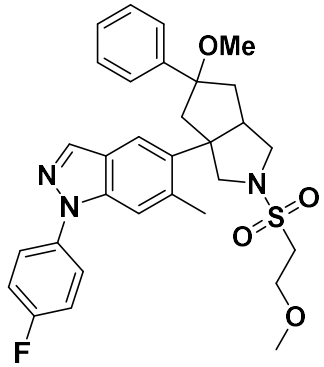

Or

;

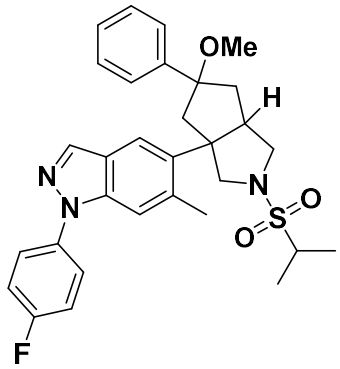


Or ;

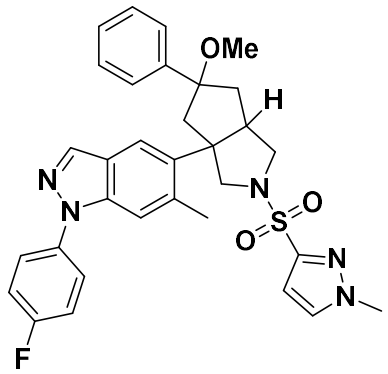

;

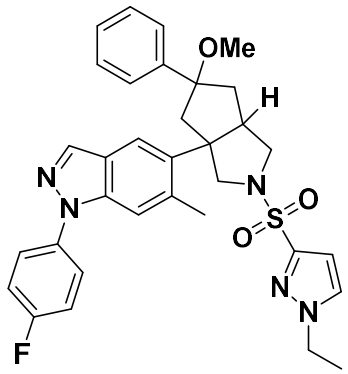

;

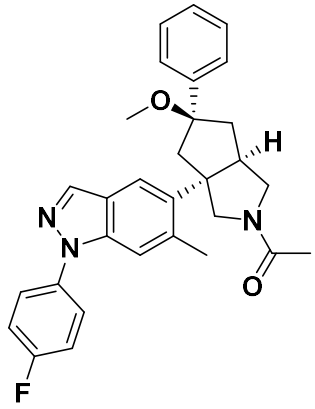
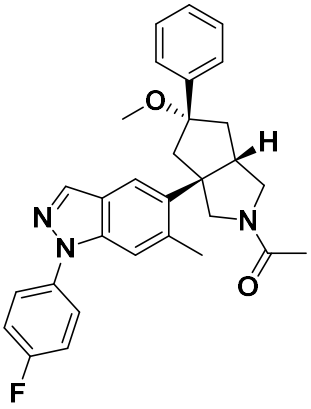

;

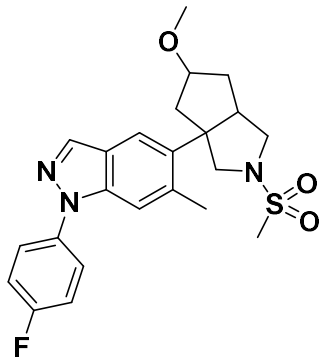

OMe
N
N
N
S
O
O
O
F
;

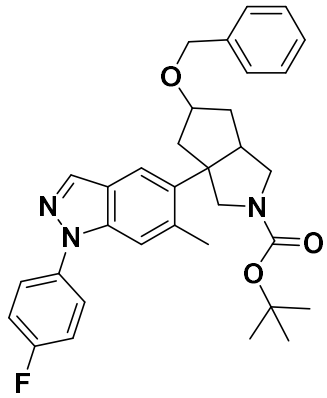

OMe
H
N
N
N
S
O
O
O
F
;

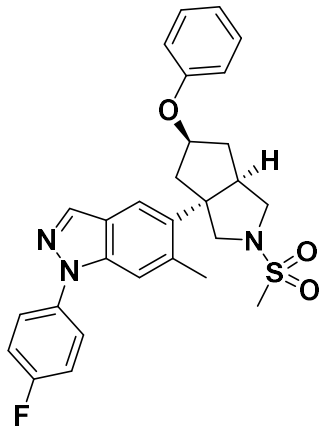

OMe
H
N
N
N
S
O
O
O
N
N
F
;

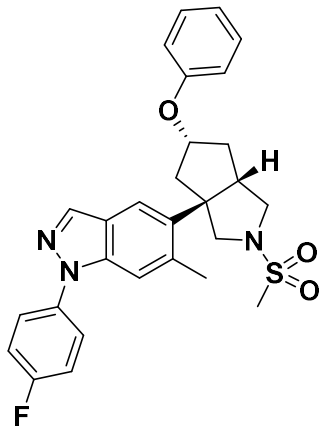

OMe
H
N
N
N
S
O
O
O
N
N
F
;

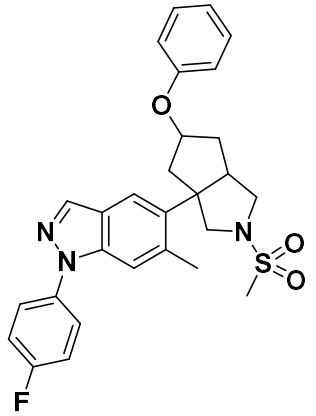


Or ;

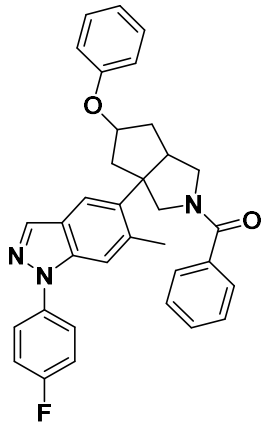

;

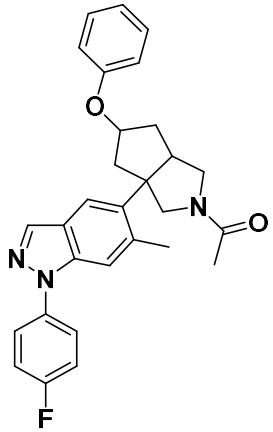

;

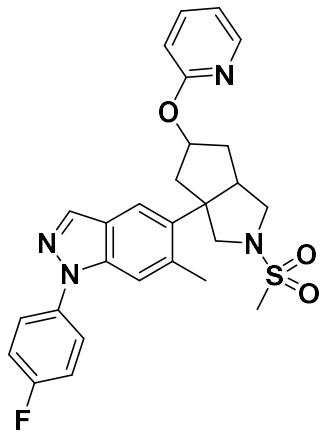

;

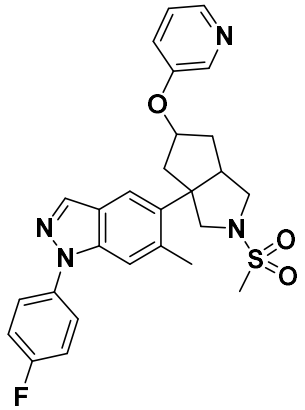

O
H
N
N
N
S
O
O
F
;

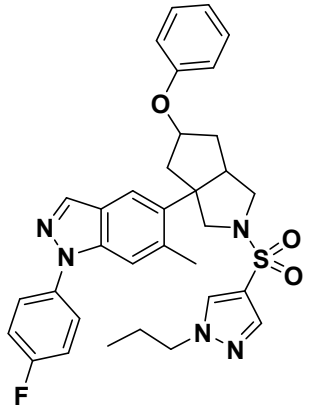

O
N
N
N
S
O
O
F
;

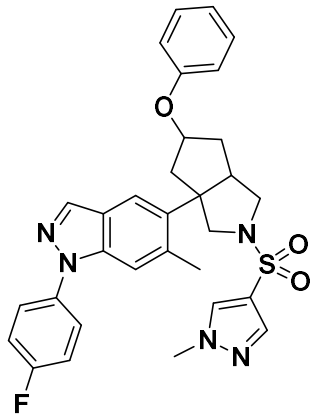

O
N
N
N
O
F
;

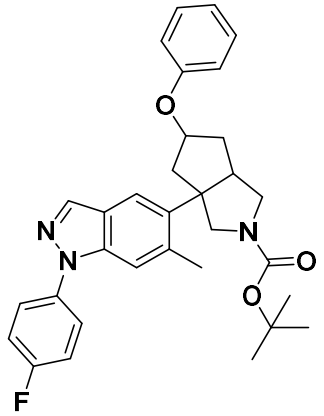

O
N
N
N
O
F
;

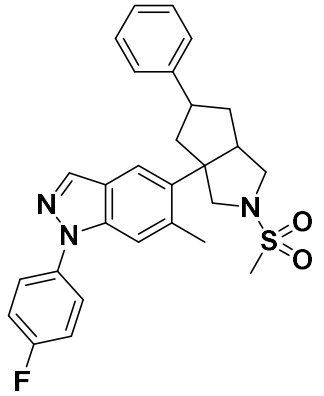

N
O
N
N
N
S
O
O
F
;

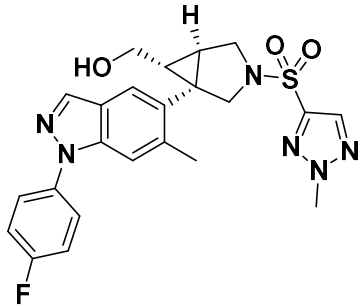
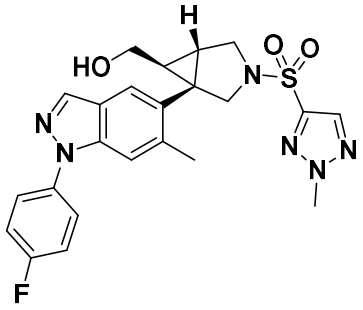

N
O
N
N
N
S
O
O
F
;

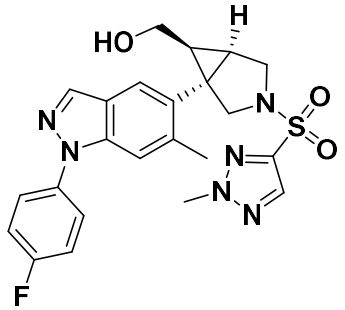
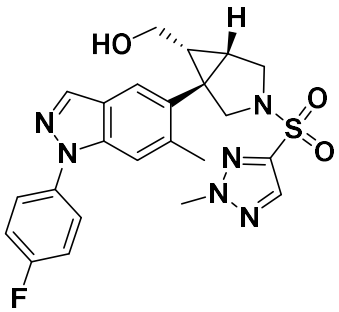

O
N
N
N
S
O
O
N
N
F
;

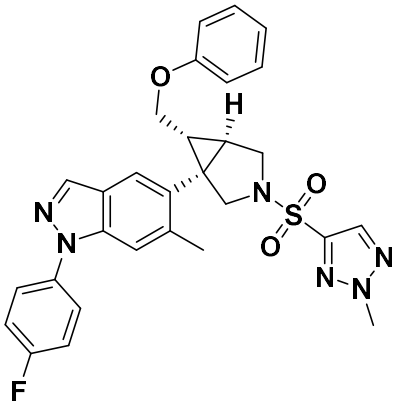
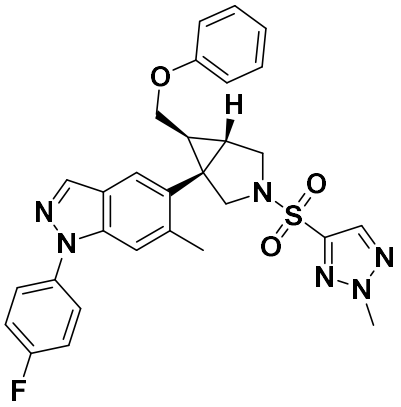

O
N
N
N
S
O
O
N
N
F
;

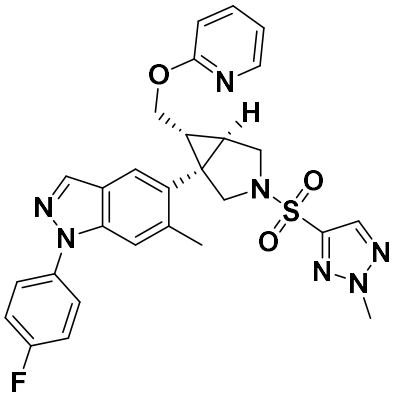
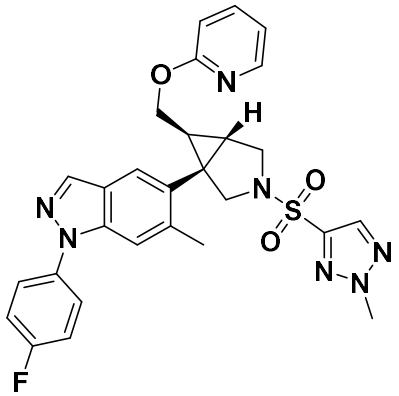

;

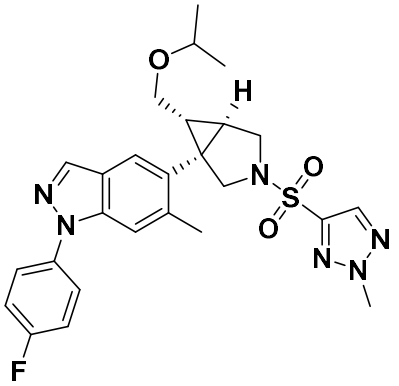
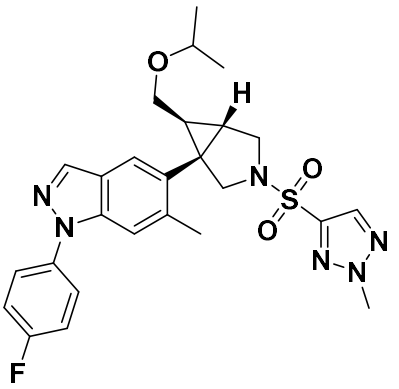

;

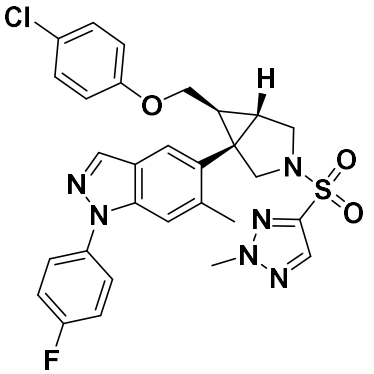

And

;

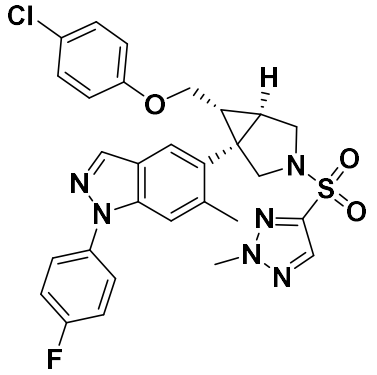


;

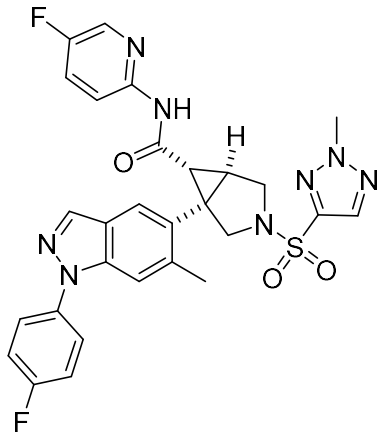
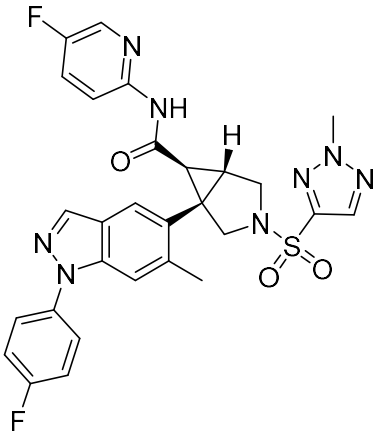


;

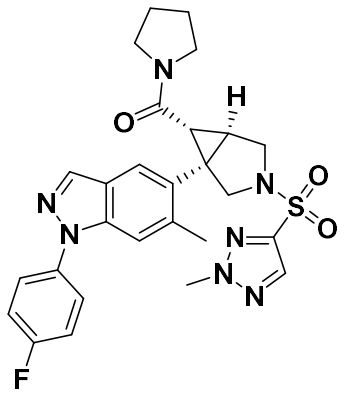
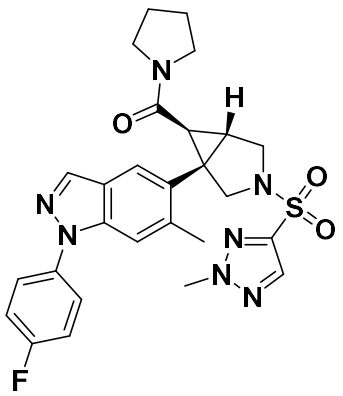


;

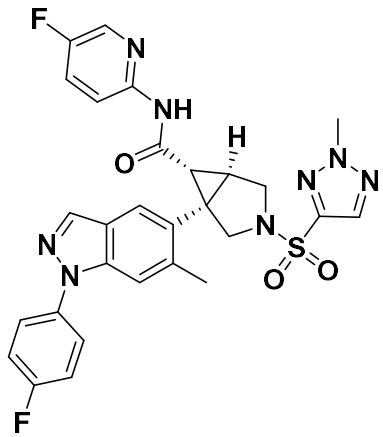


;

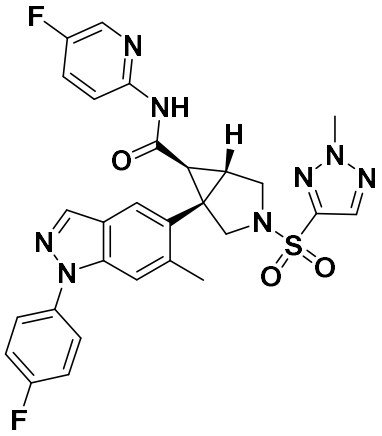

;

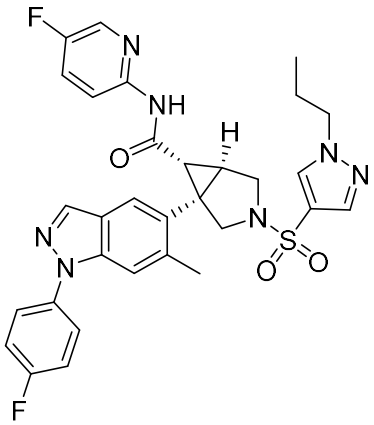
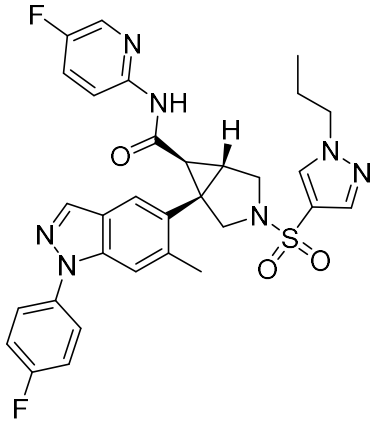

Cl
O
H
N
S
O
O
N
N
N
N
N
F
;

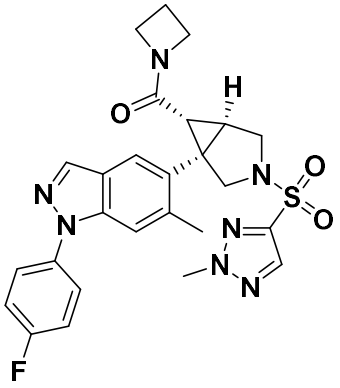
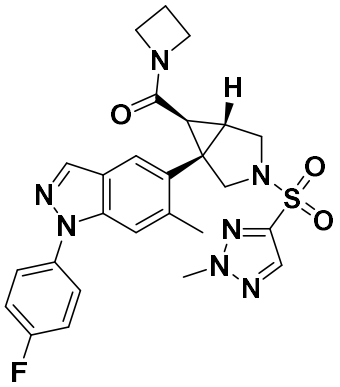

F
N
NH
O
H
N
N
N
N
S
O
O
N
N
F

F
N
NH
O
H
N
N
N
N
S
O
O
N
N
F
;

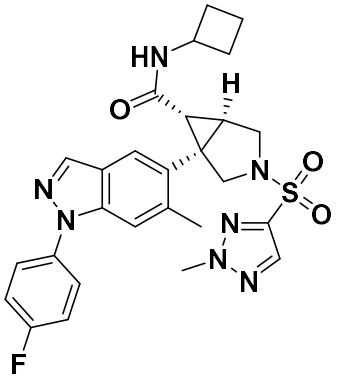
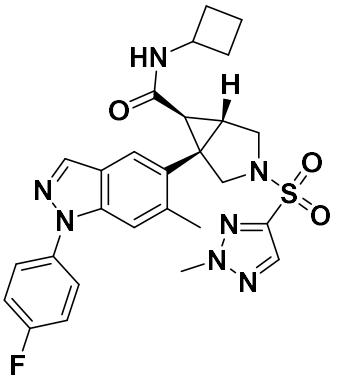

N
O
H
N
S
O
O
N
N
N
N
N
F

N
O
H
N
S
O
O
N
N
N
N
N
F
;

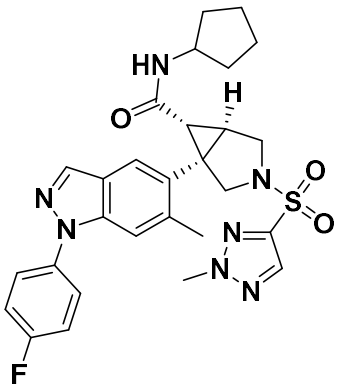
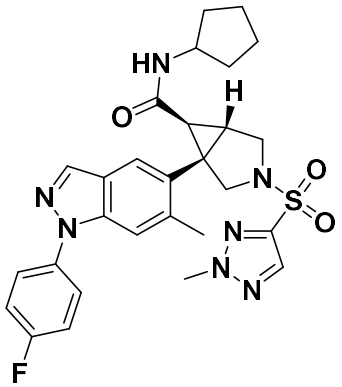

F
N
NH
O
H
N
N
N
N
S
O
O
N
N
F
;

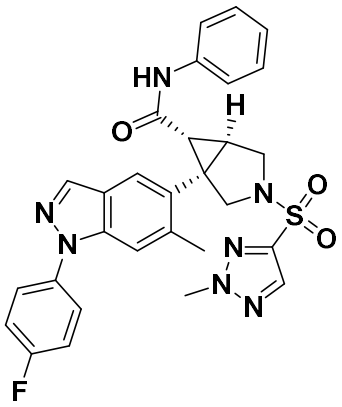
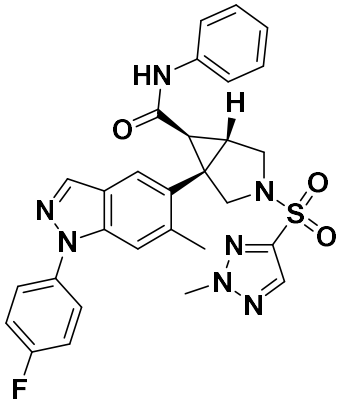

;

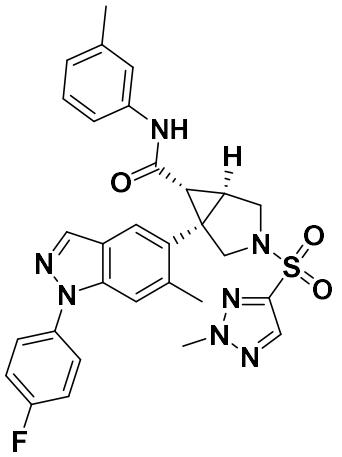
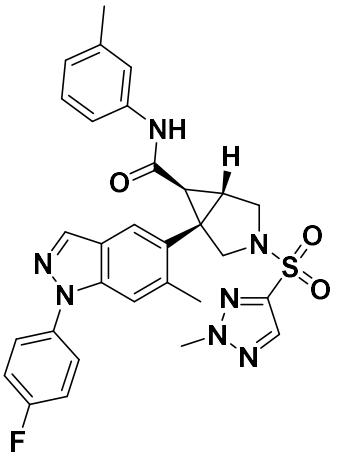


;

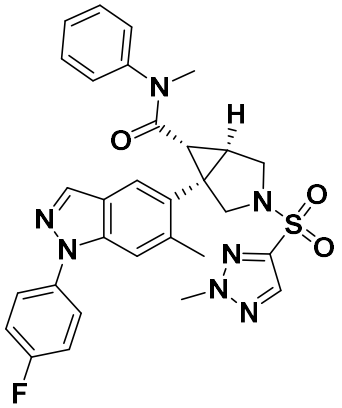
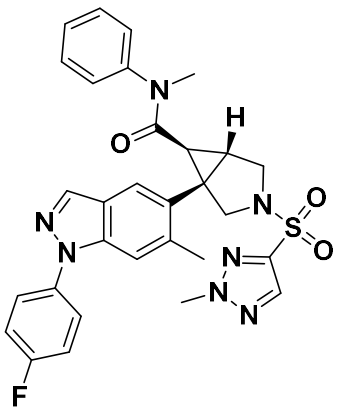


;

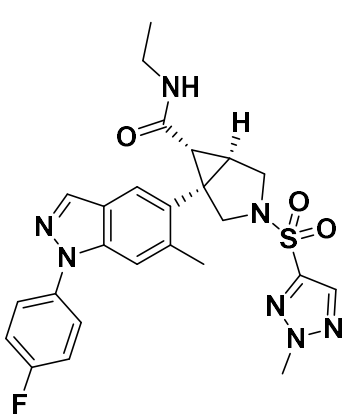
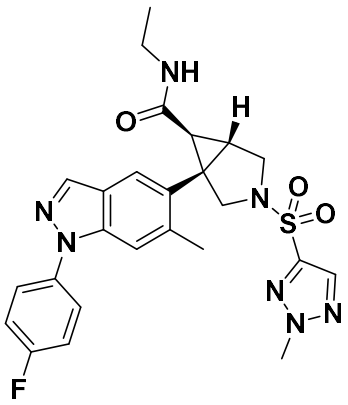


;

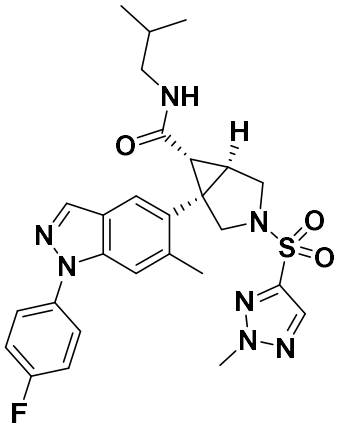
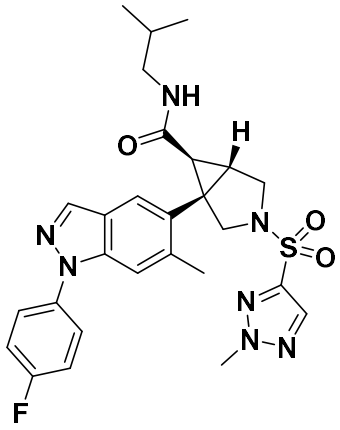


;

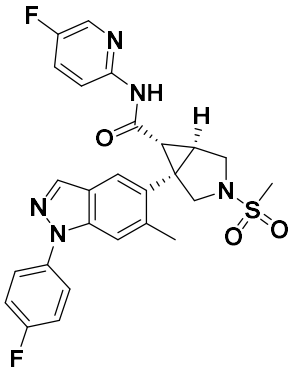
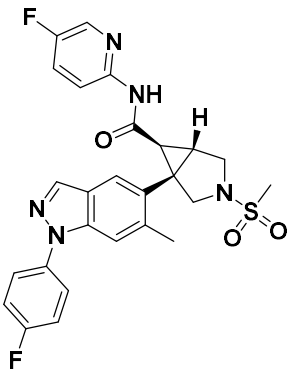


;

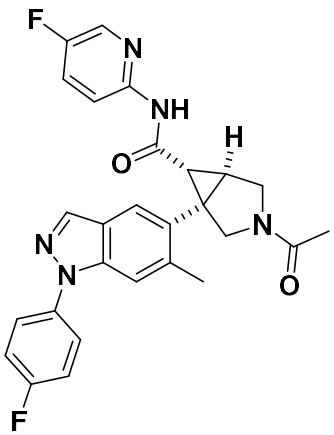
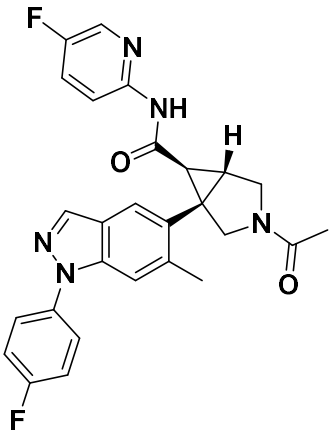


;

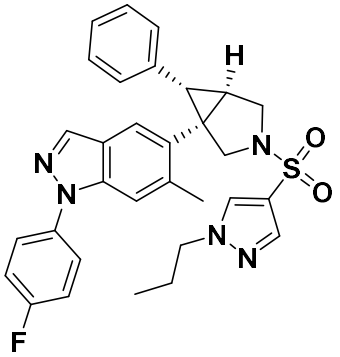
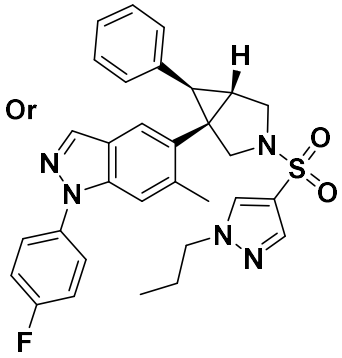


;

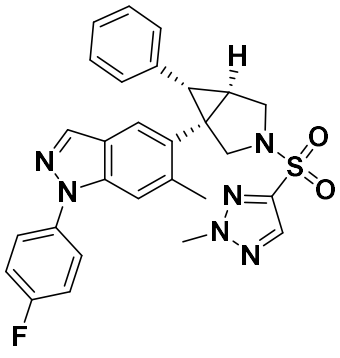
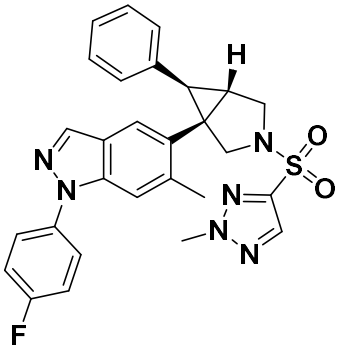


;

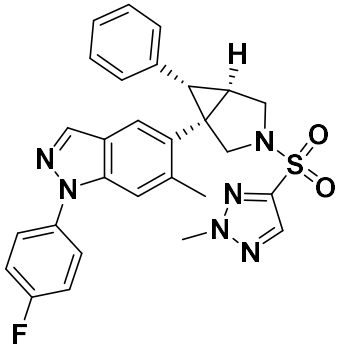
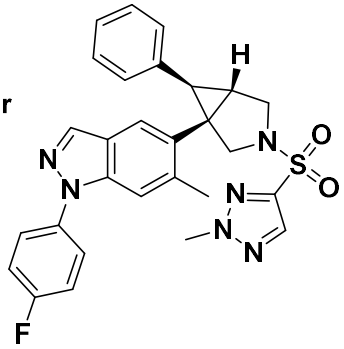


;

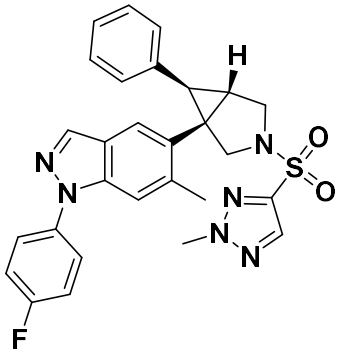
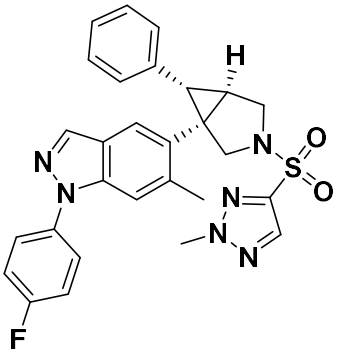


;

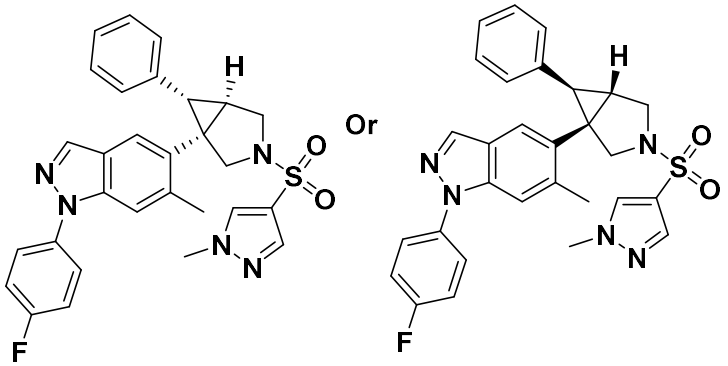


;

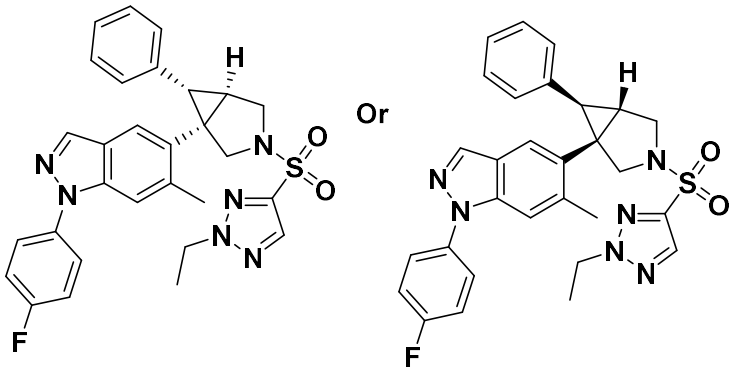


;

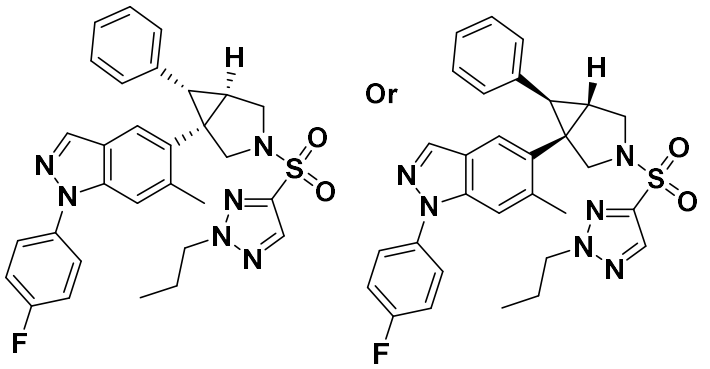


;

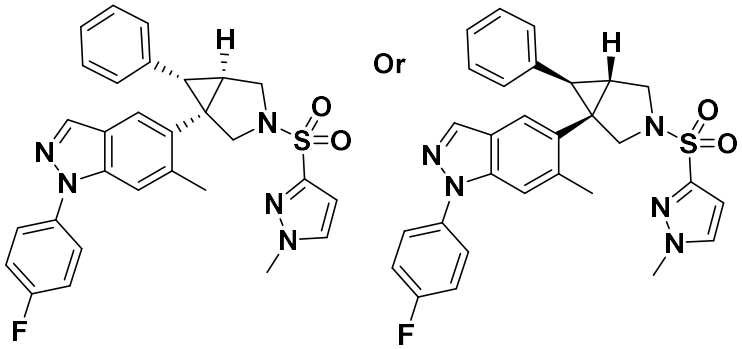

Or

;

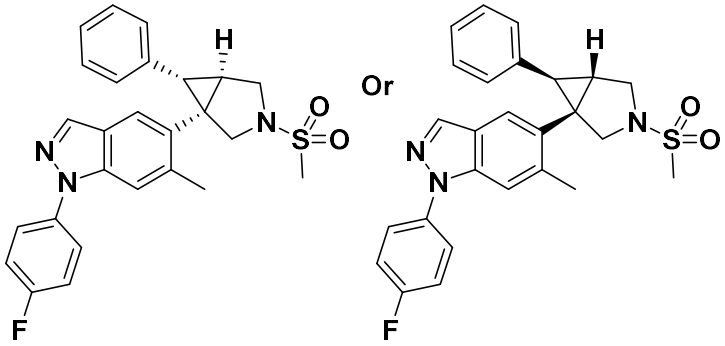

Or

;

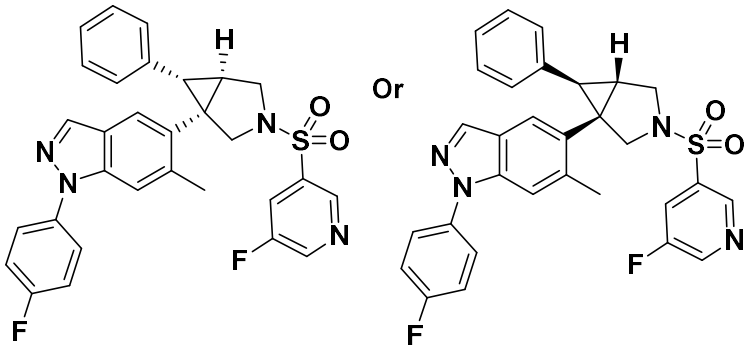

Or
;

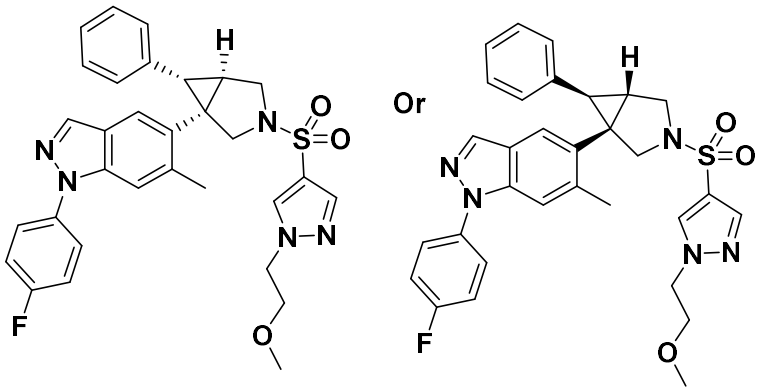

Or
;

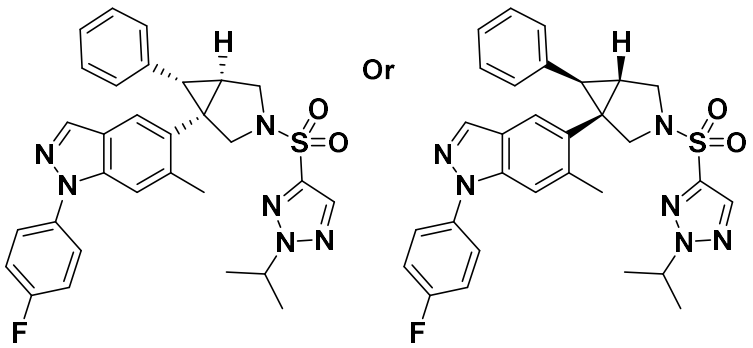

Or
;

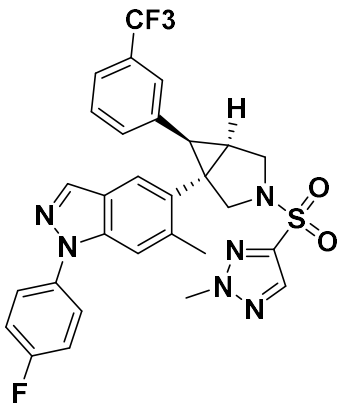
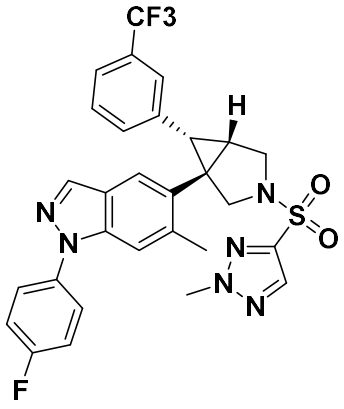

Or
;

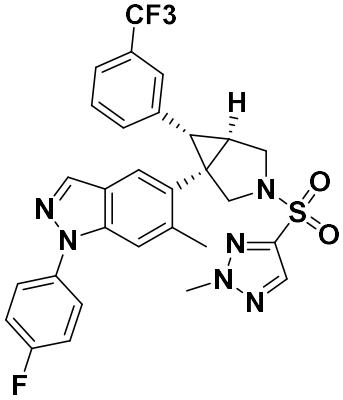
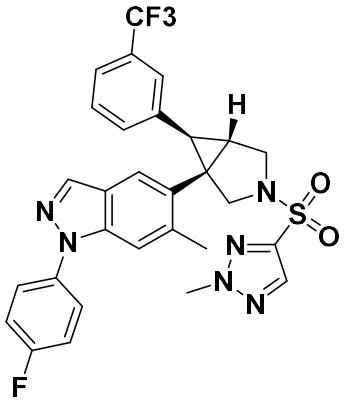

Or
;

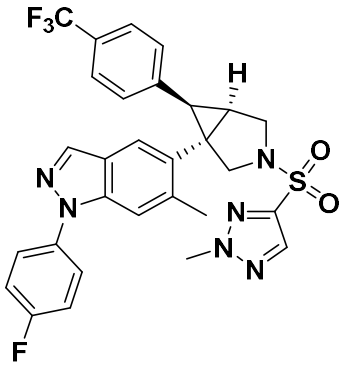
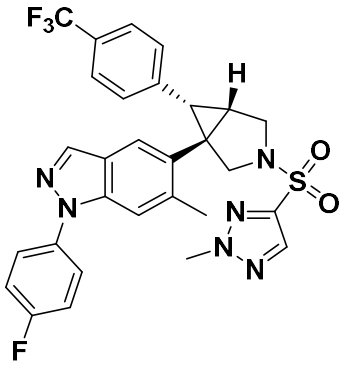

Or
;

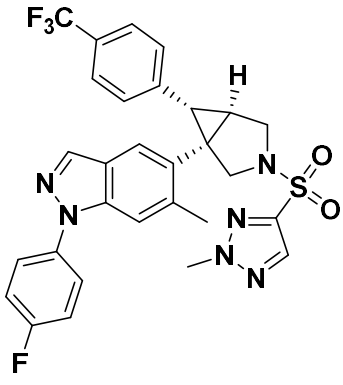
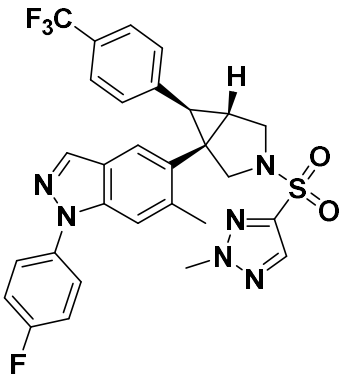

Or
;

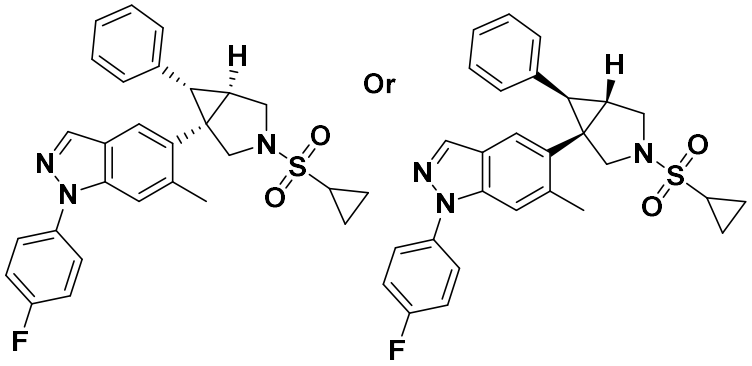

Or
;

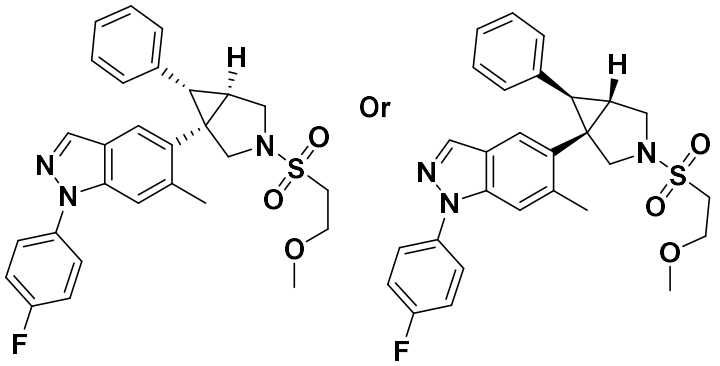


;

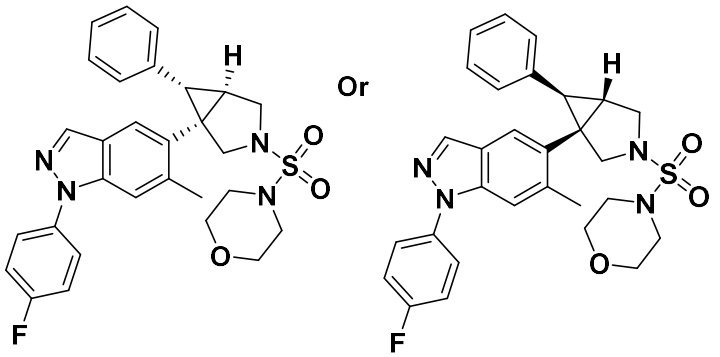


;

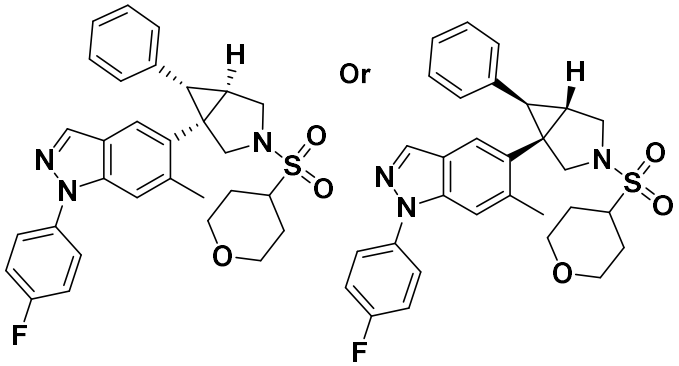


;

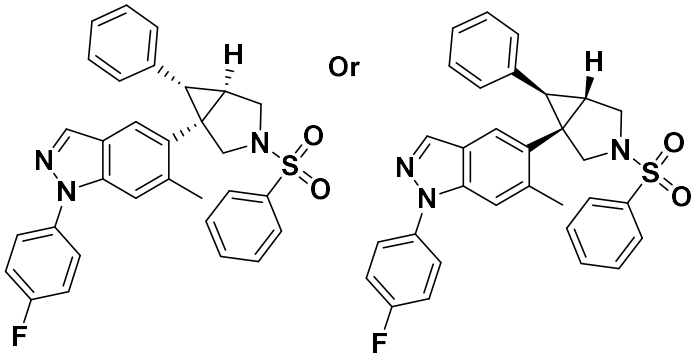


;

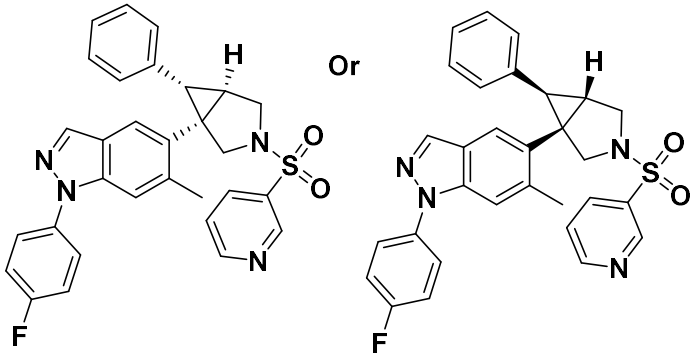

Or
;

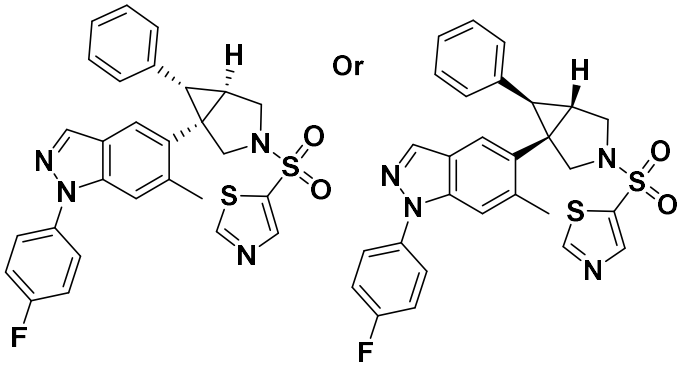

Or
;

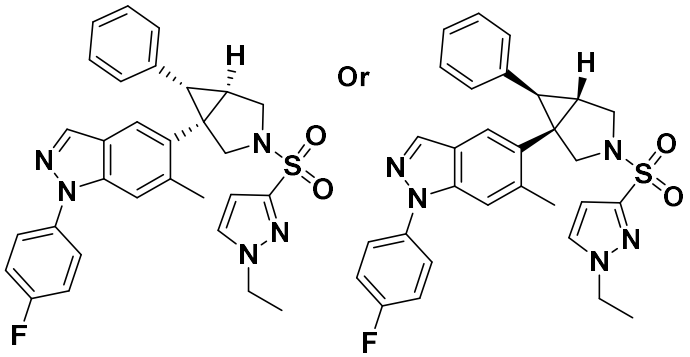

Or
;

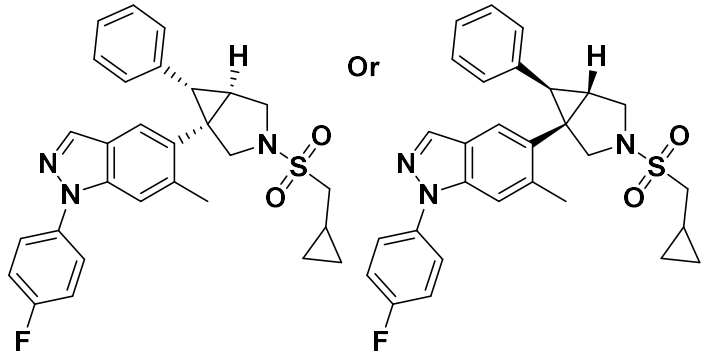

Or
;

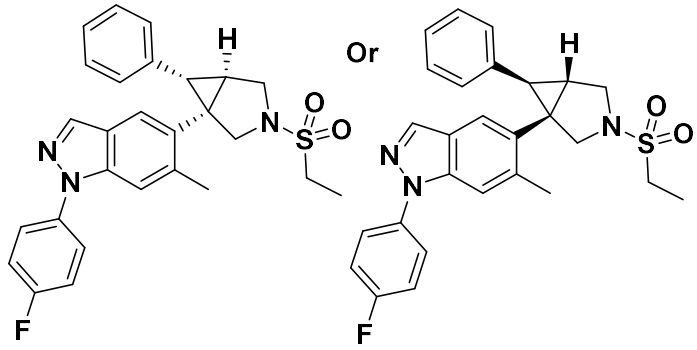

Or
;

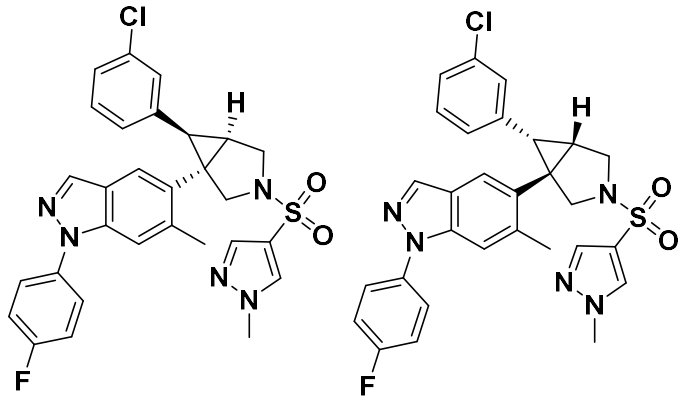

Or
;

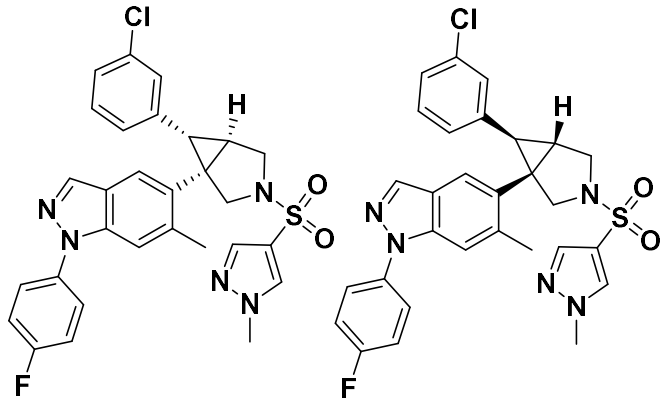

Or
;

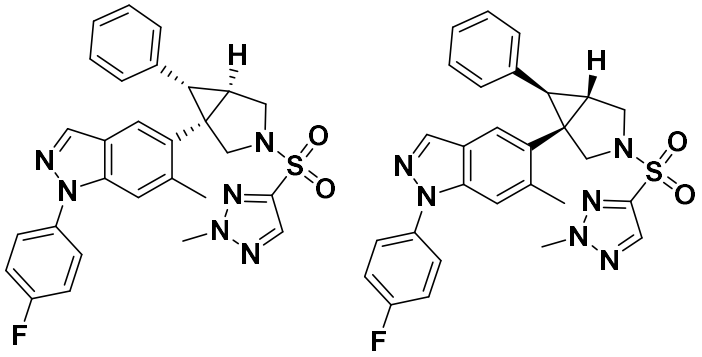

Or
;

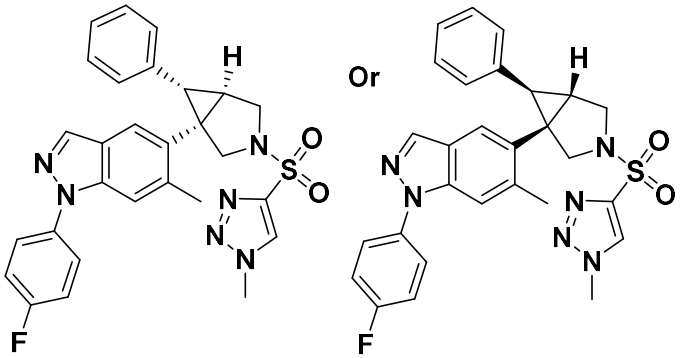

H
Or
H
N
N
S
O
O
N
N
S
O
O
F
F
;

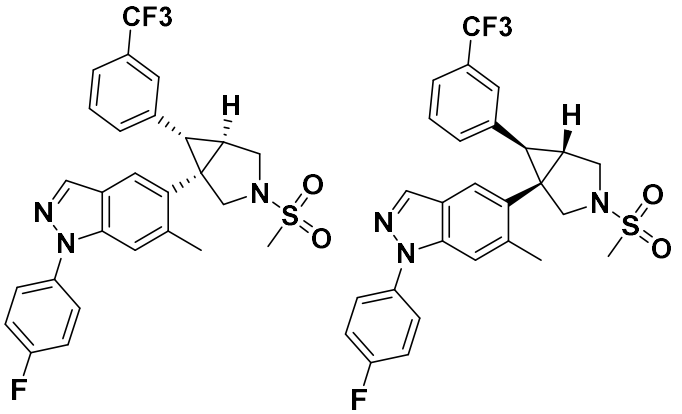

H
Or
H
N
N
S
O
O
N
N
S
O
O
F
F
;

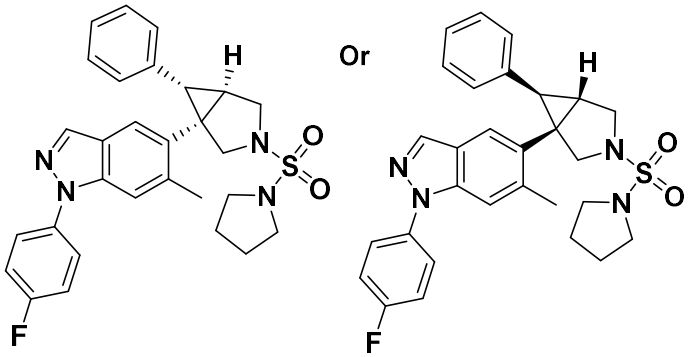

Cl
Cl
H
H
N
N
S
O
O
N
N
S
O
O
N
N
N
N
F
F
;

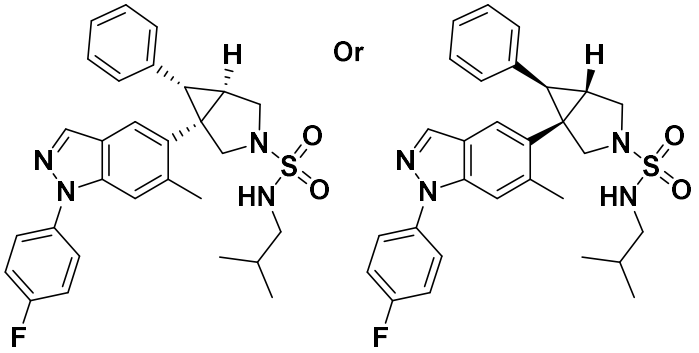

Cl
Cl
H
H
N
N
S
O
O
N
N
S
O
O
N
N
N
N
F
F
;

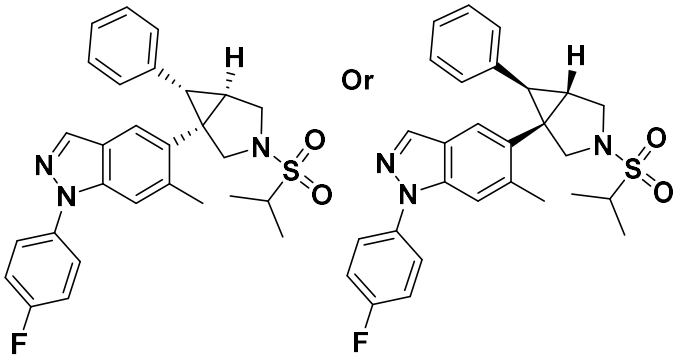

;

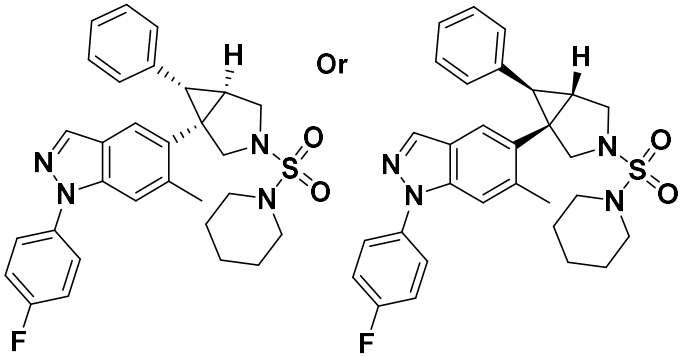

;

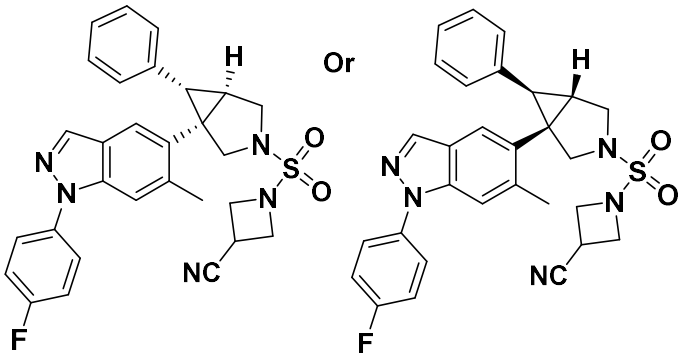

;

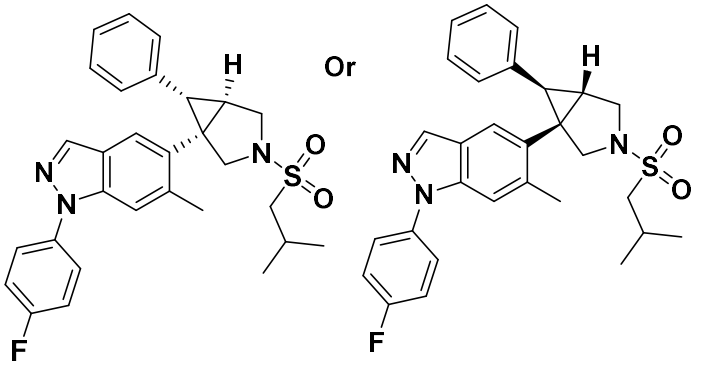

;

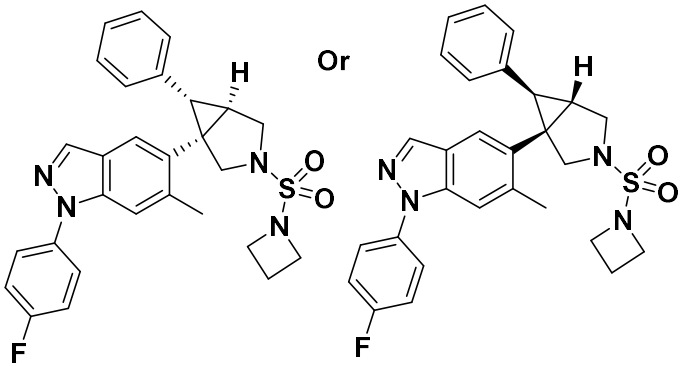

Or
;

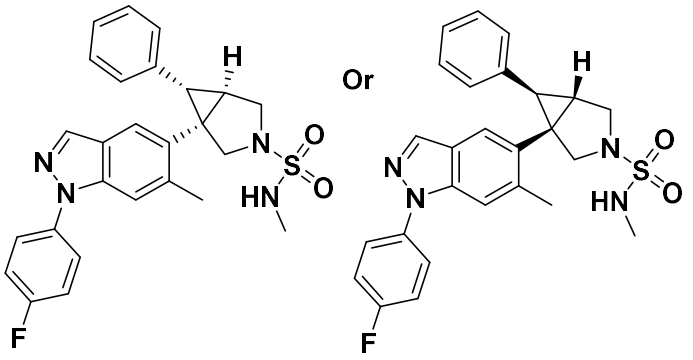

Or
;

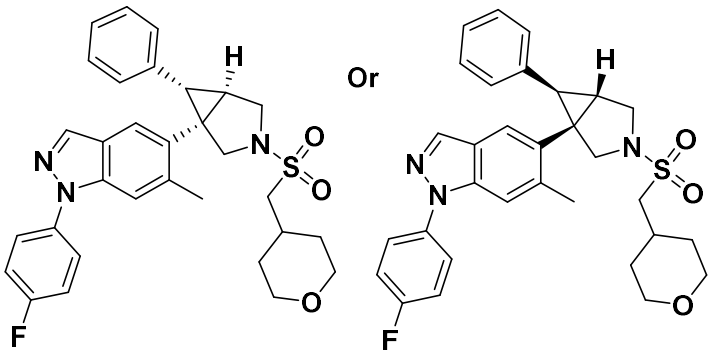

Or
;

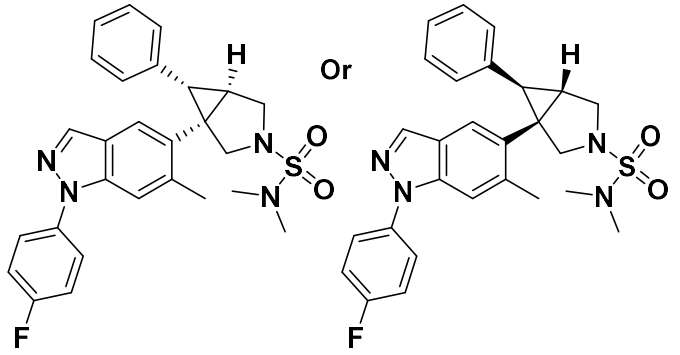

Or
;


Or
;

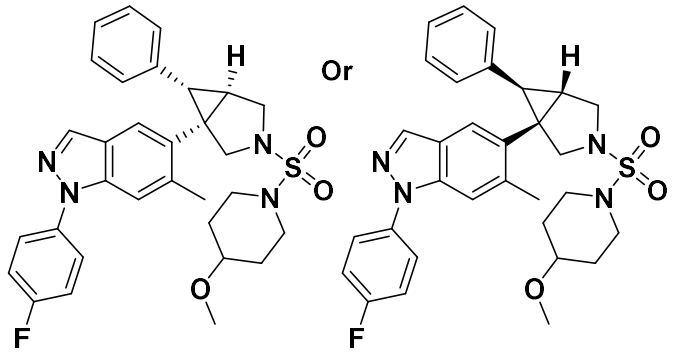

Or
;


Or
;

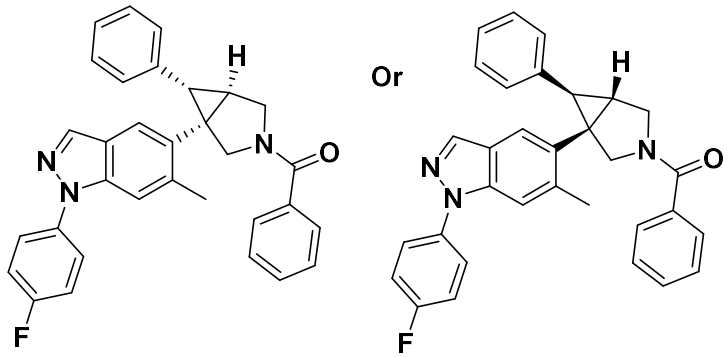

Or
;



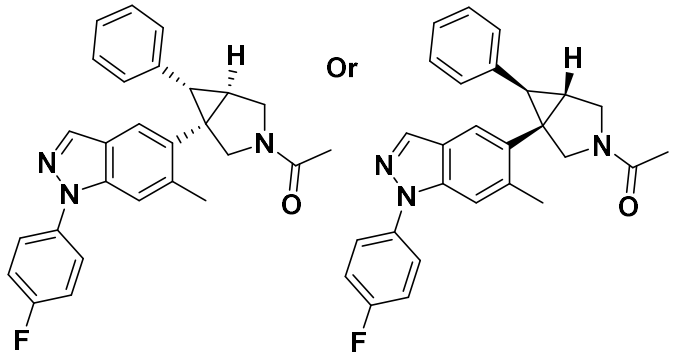
;



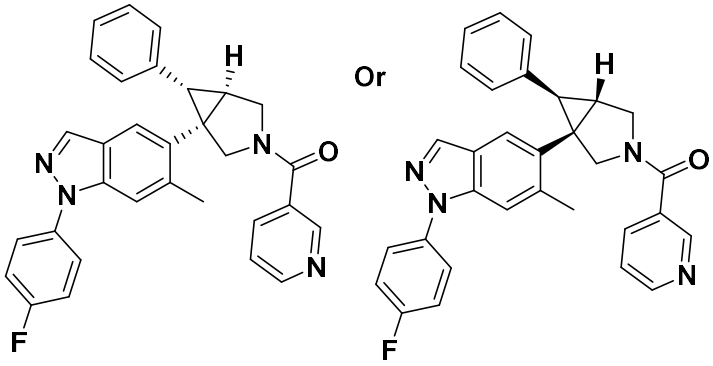
;

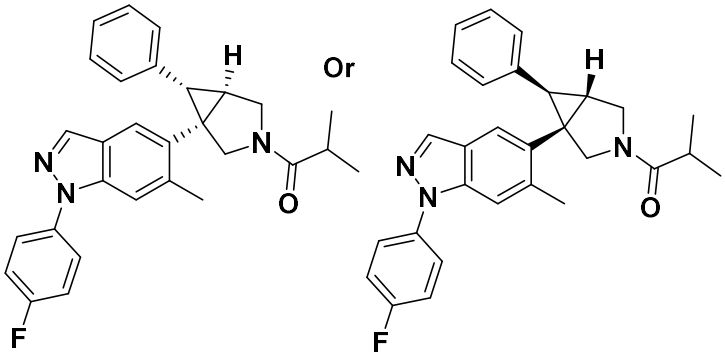


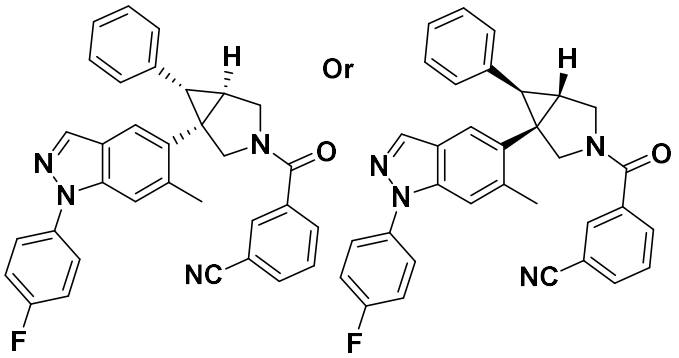
;

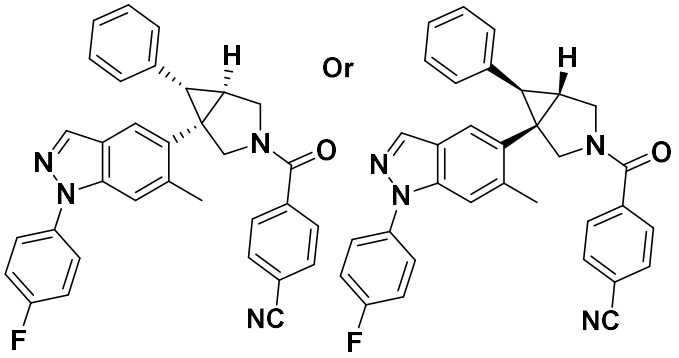


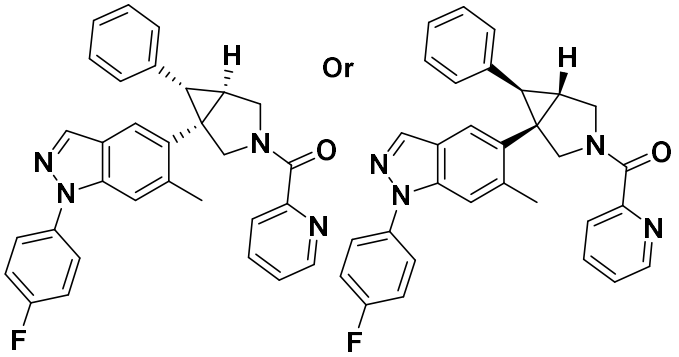
;

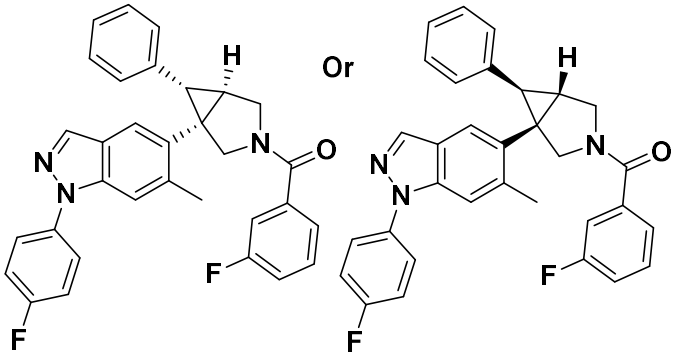

Or
;

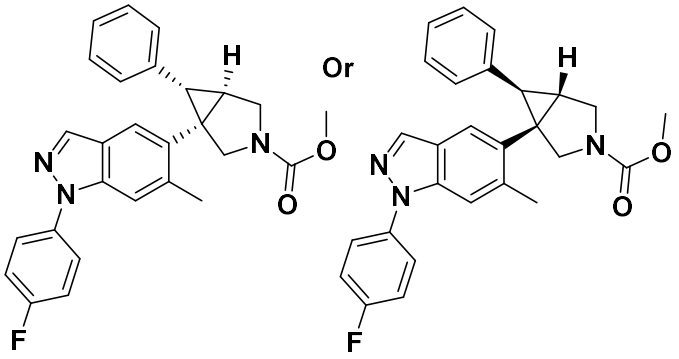

Or
;

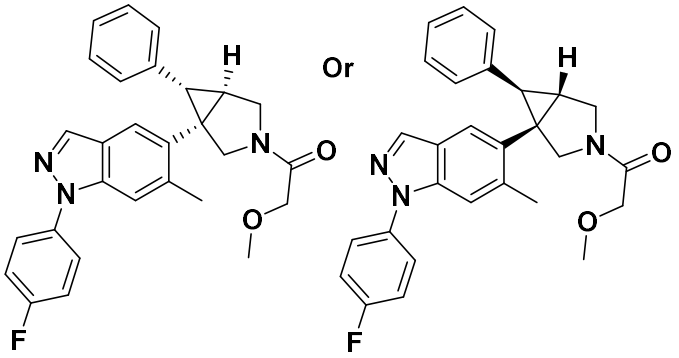

Or
;

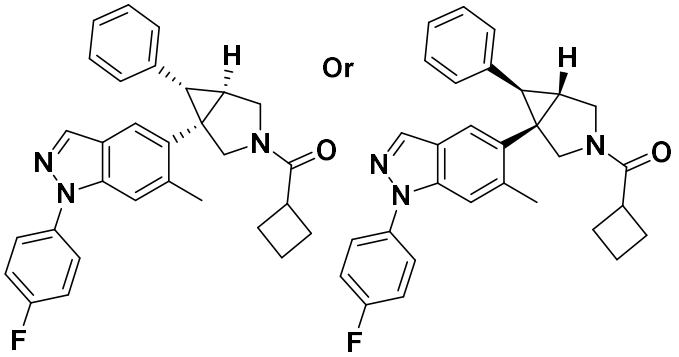

Or
;

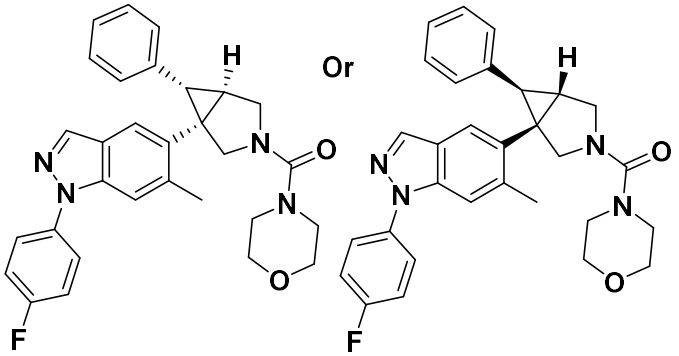

Or
;

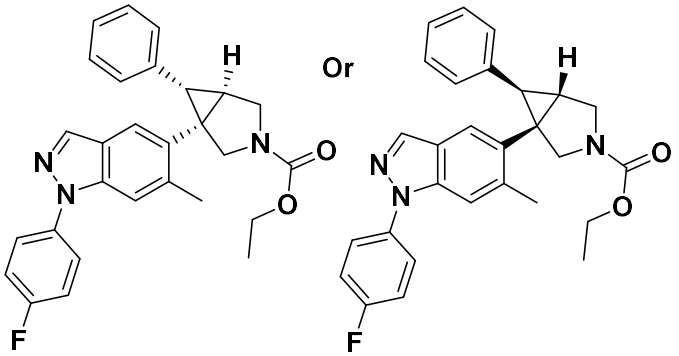

Or
;

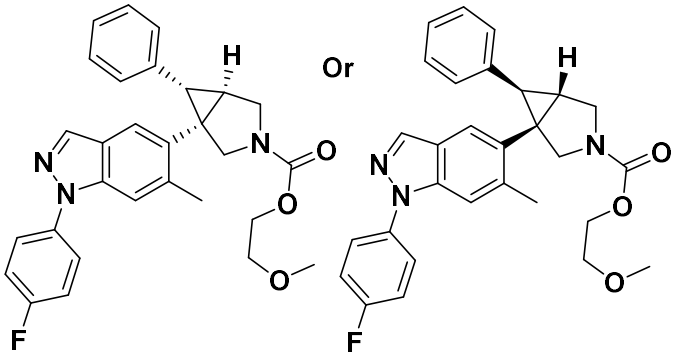

Or
;

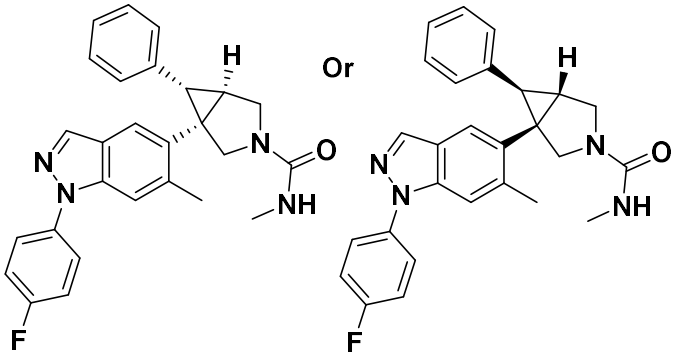

Or
;

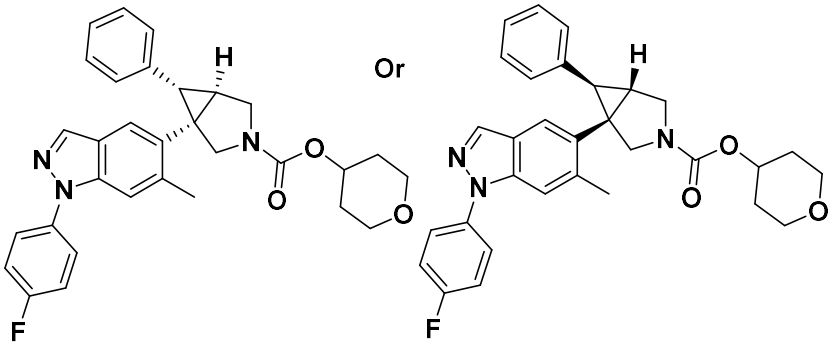

H
Or
H
N
O
N
N
N
O
F
F
;

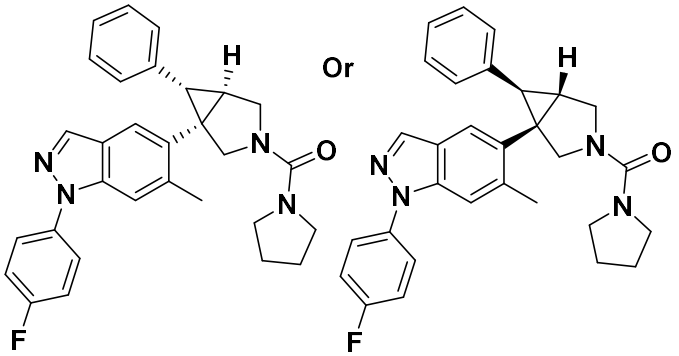

H
Or
H
N
O
N
N
N
N
O
O
F
F
;

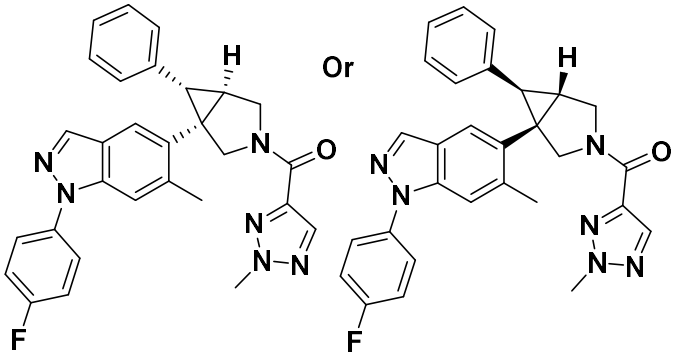

H
Or
H
N
O
N
N
N
O
O
F
F
;

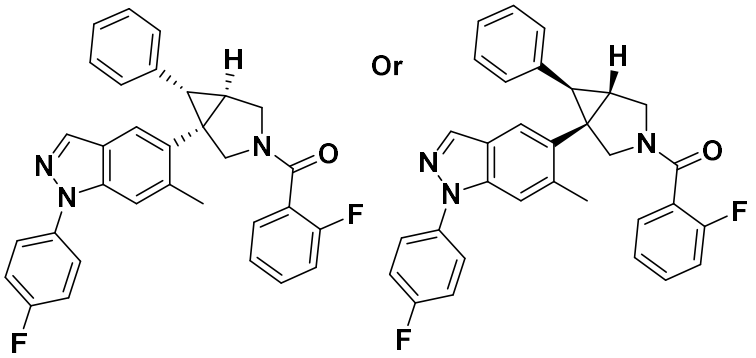

H
Or
H
N
O
N
N
N
O
O
O
F
F
;

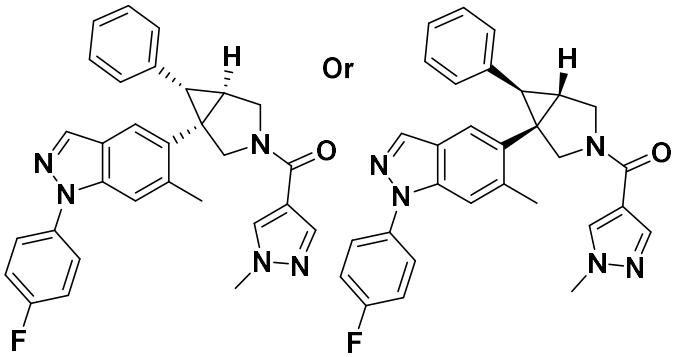

H
Or
H
N
O
NH
N
N
F
;

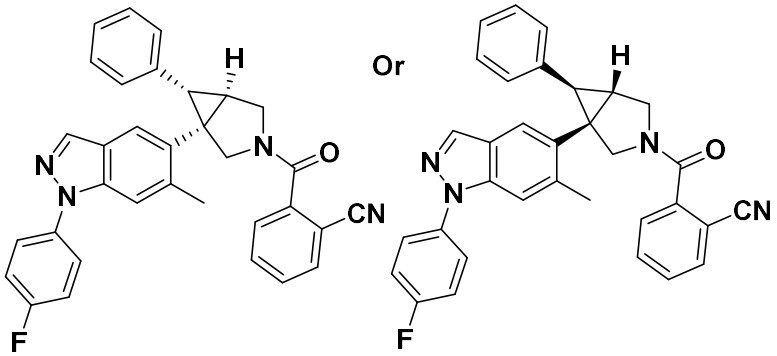

H
Or
H
N
O
O
O
N
N
F
;

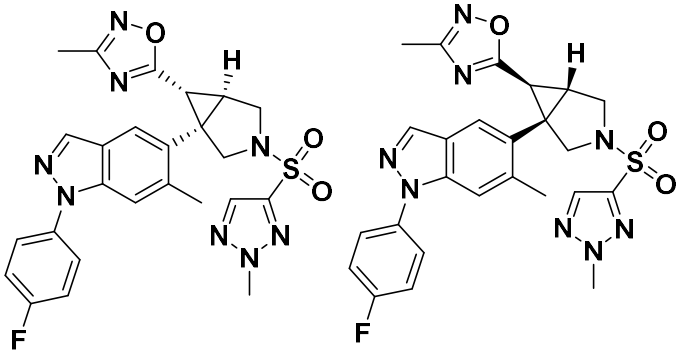

H
Or
H
N
O
N
N
F
;

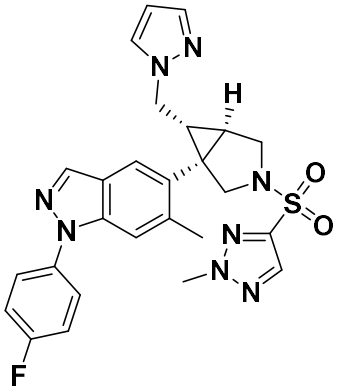
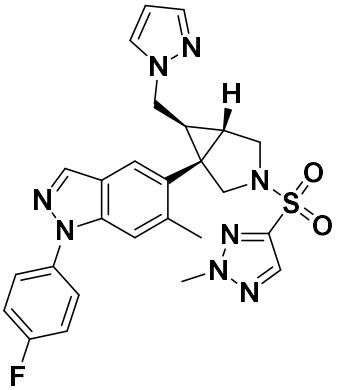

H
Or
H
N
O
N
N
N
N
F
;

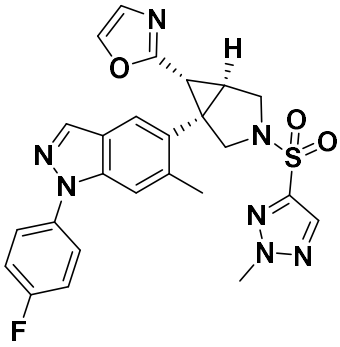
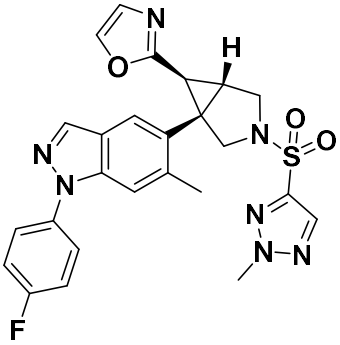

Or
;

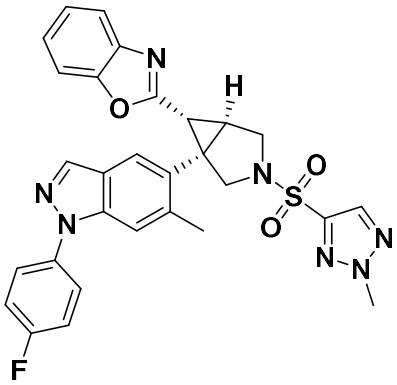
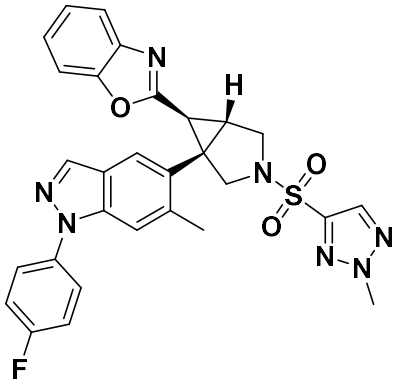

Or
;

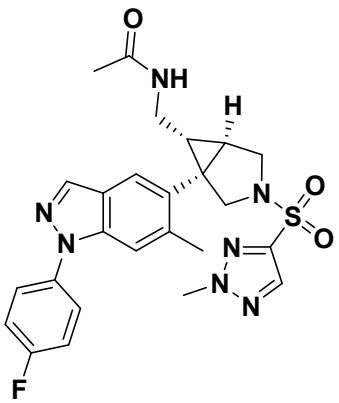
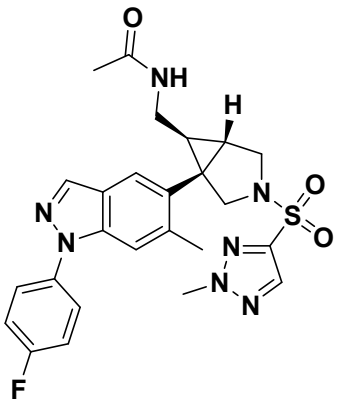

Or
;

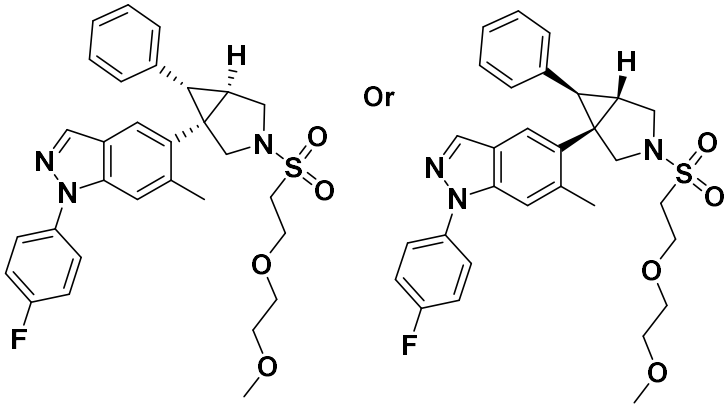

;

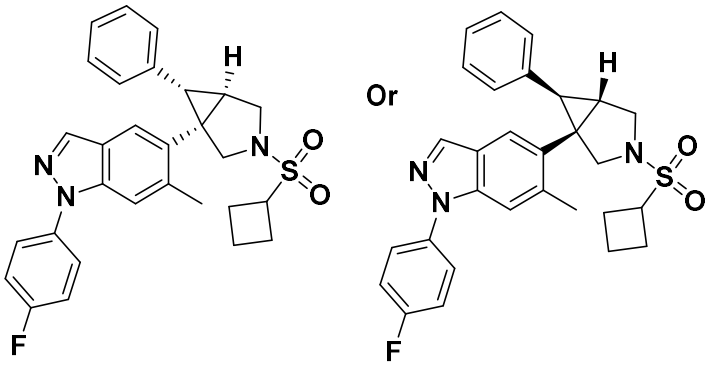


;

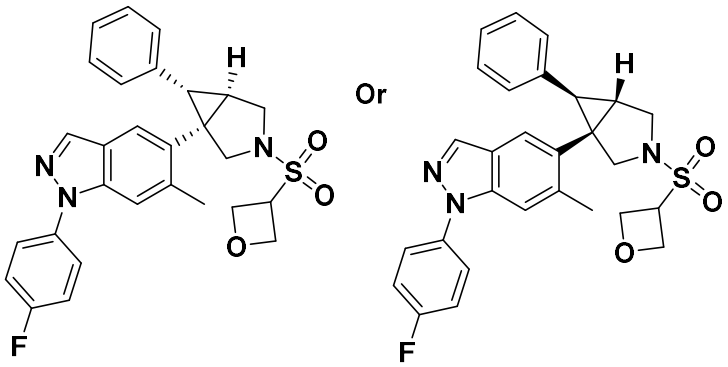


;

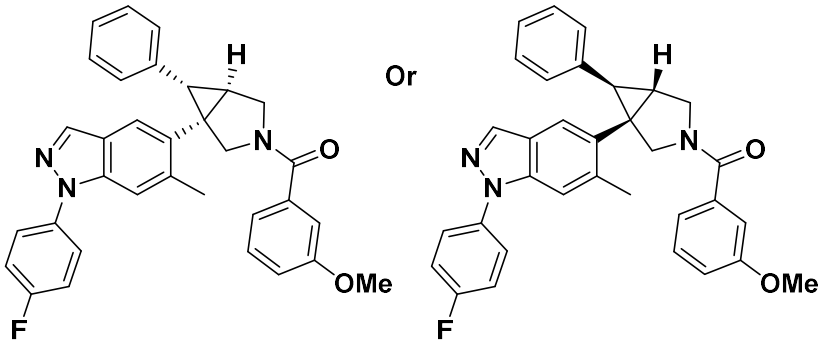


;

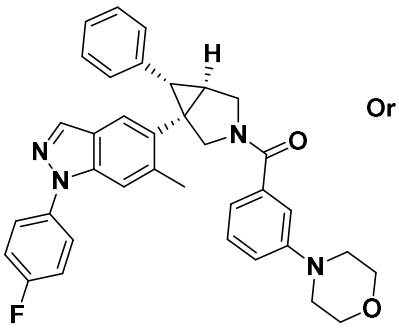
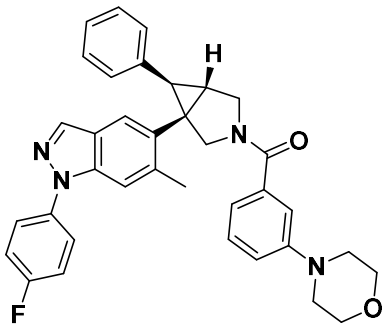


;

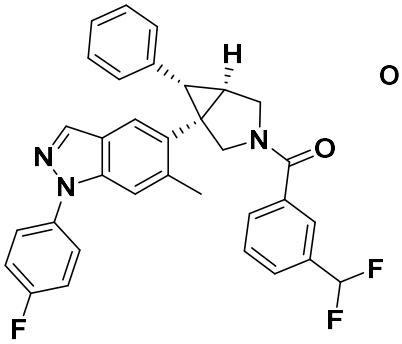
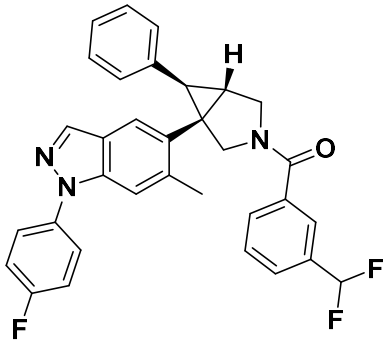

H
N
N
S
O
O
O
O
F
Or
H
N
N
S
O
O
O
O
F
;

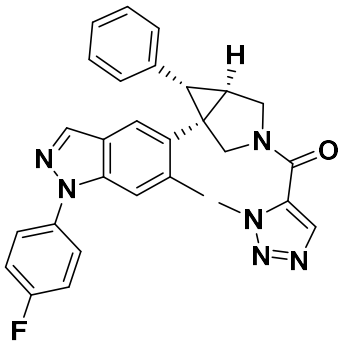
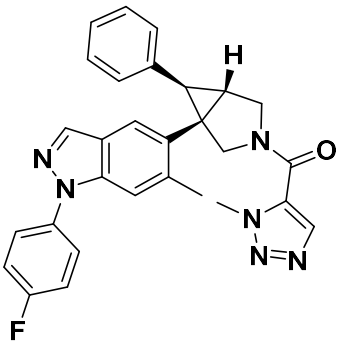

H
N
N
S
O
O
F
Or
H
N
N
S
O
O
F
;

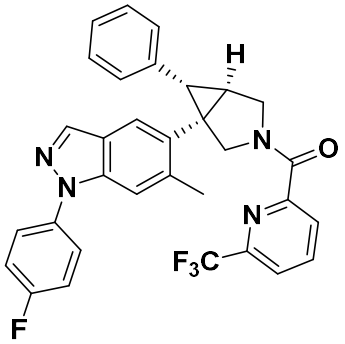
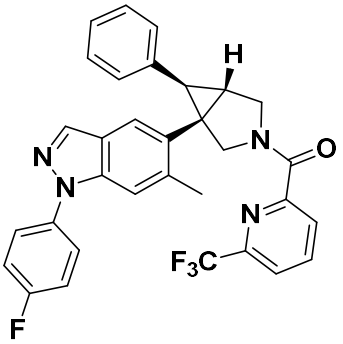

H
N
N
S
O
O
O
F
Or
H
N
N
S
O
O
O
F
;

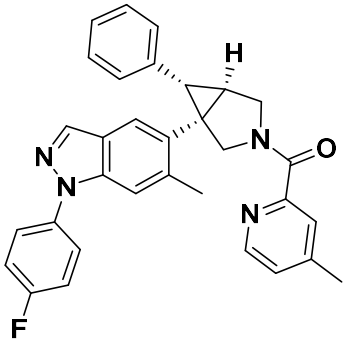
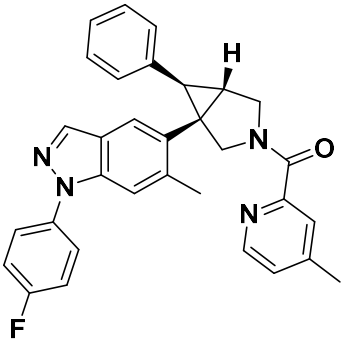

H
N
N
O
OMe
F
Or
H
N
N
O
OMe
F
;

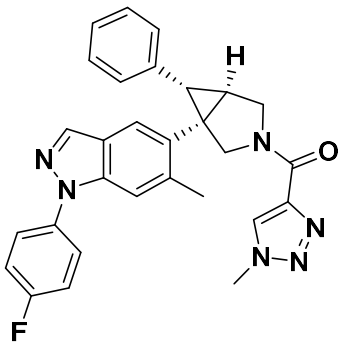
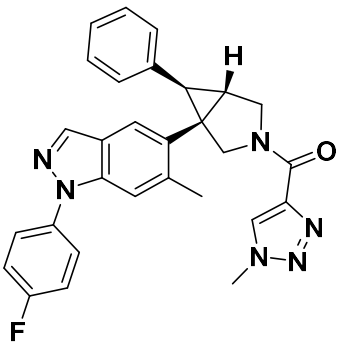

Or

;

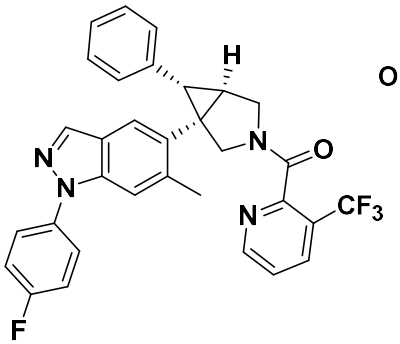
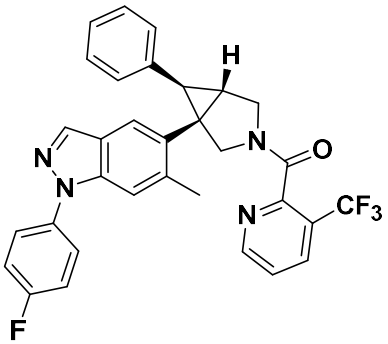

Or

;

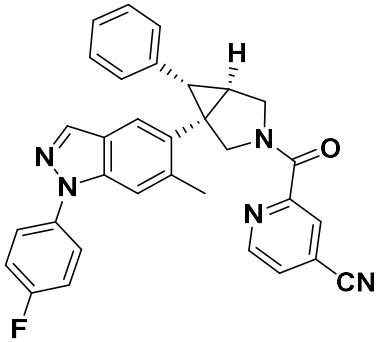
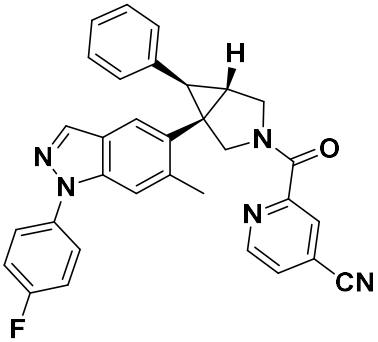

Or

;

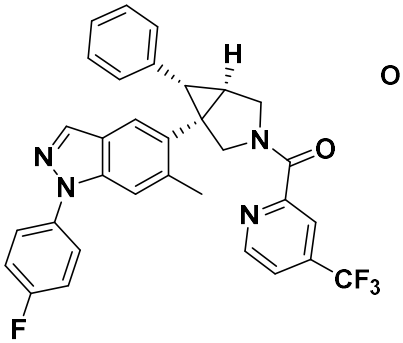
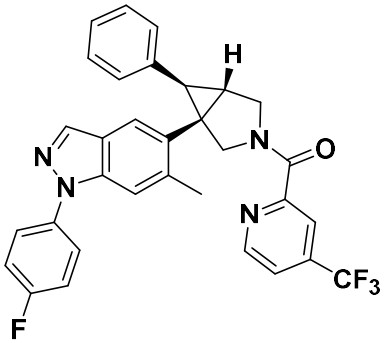

Or

;

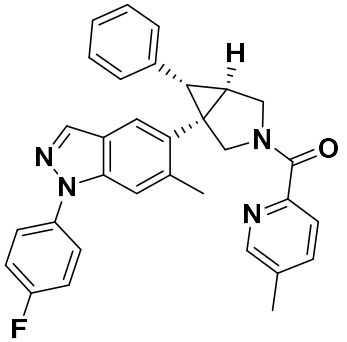
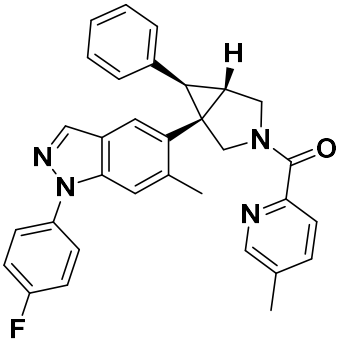

Or

;

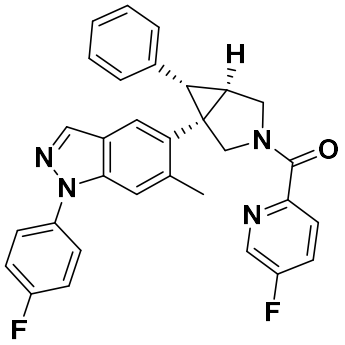
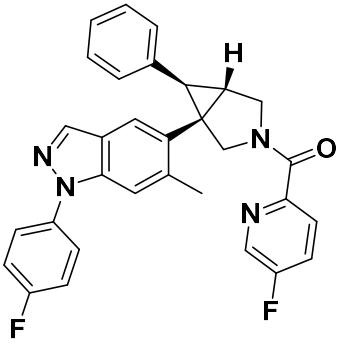

Or

;

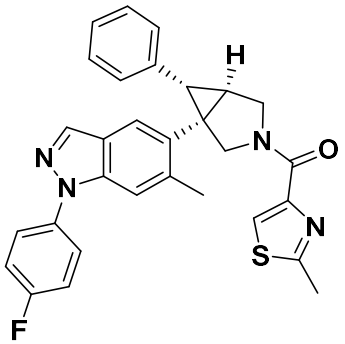
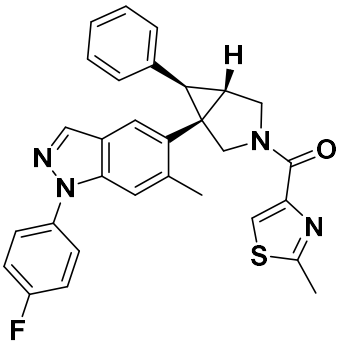

Or

;

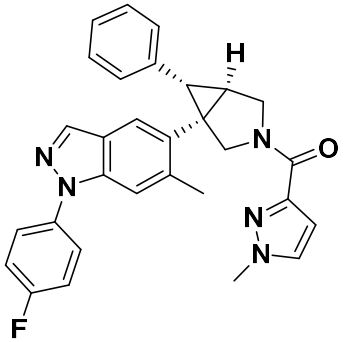
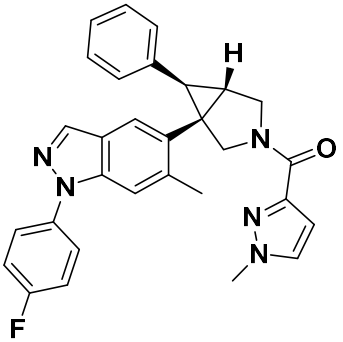

Or

;

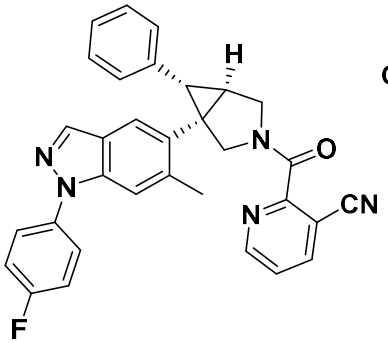
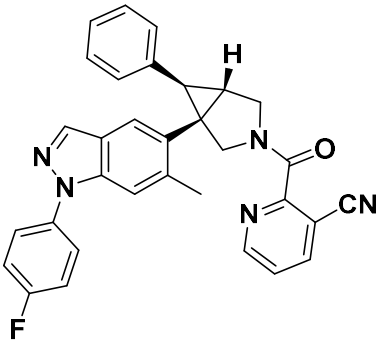

Or

;

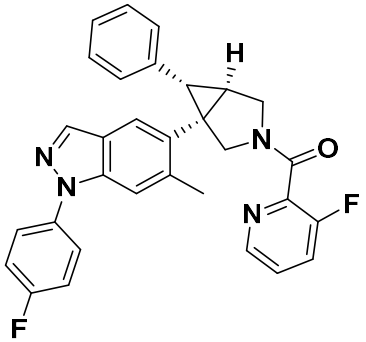
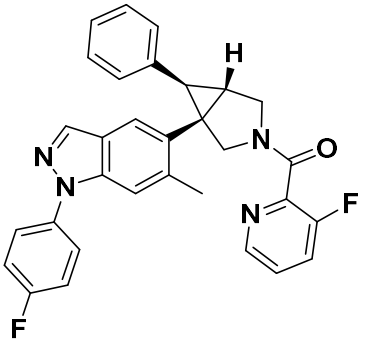

Or

;

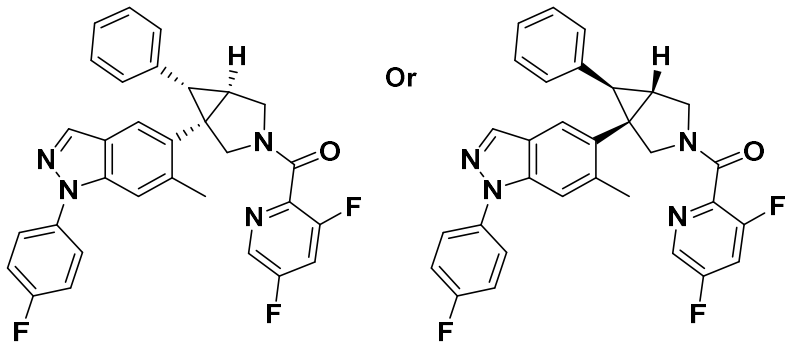

Or

;


Or

;

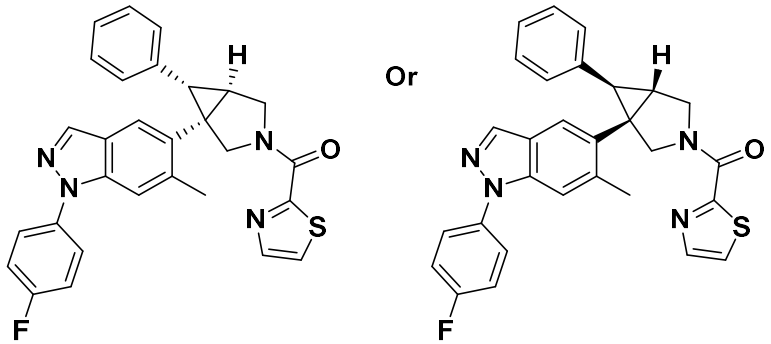

Or

;


Or

;

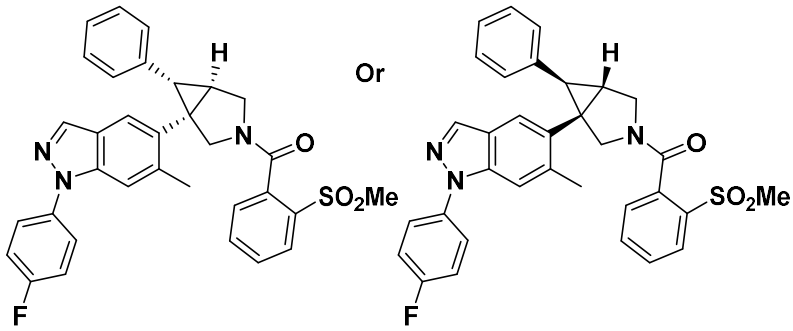

Or

;



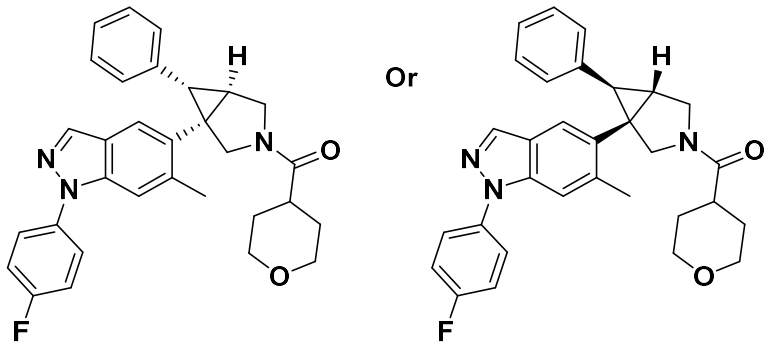
;



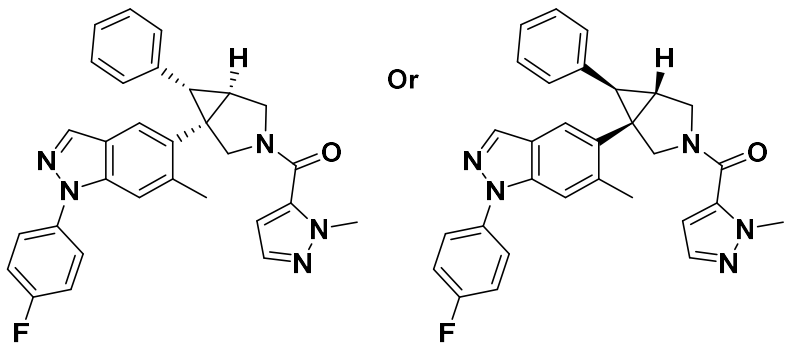
;



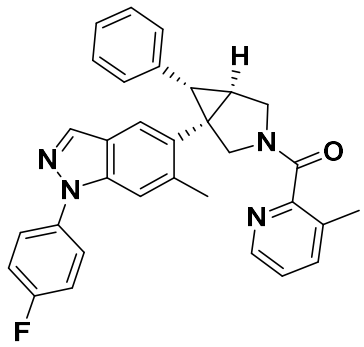
;



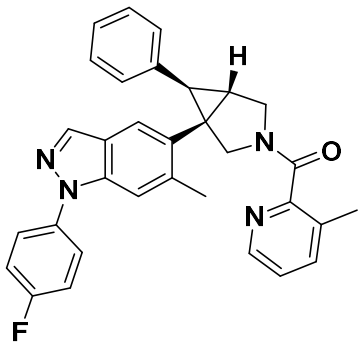
;



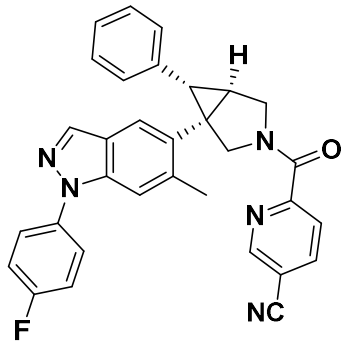
;



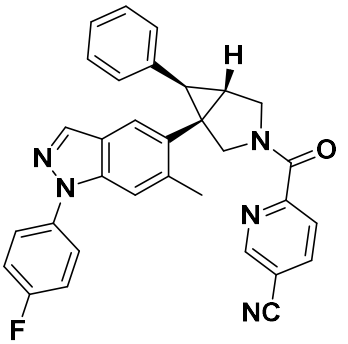
Or



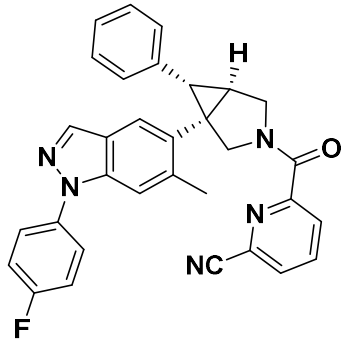
;



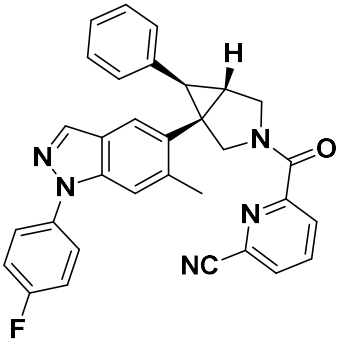
Or



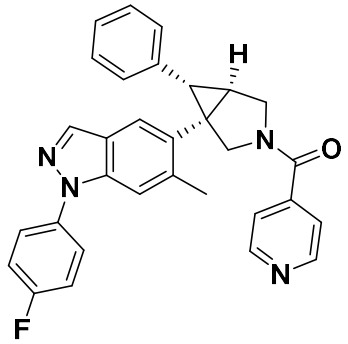
;



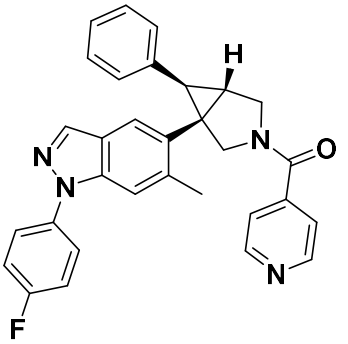
Or



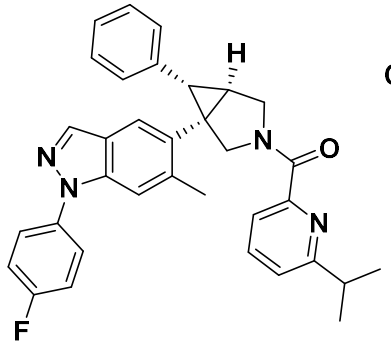
;



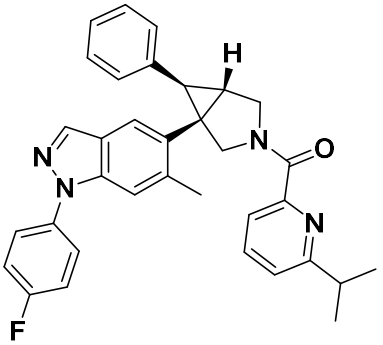
Or



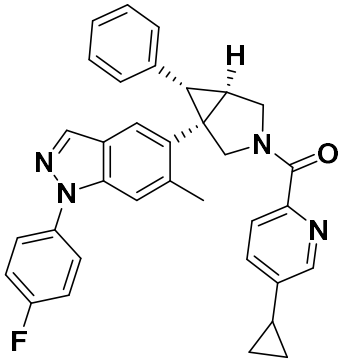
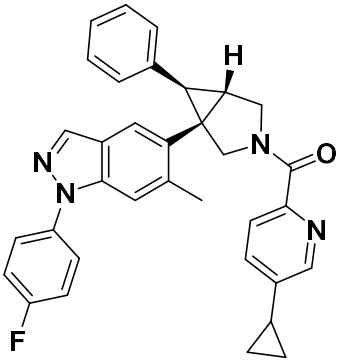
;

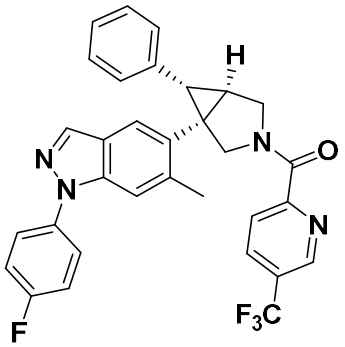
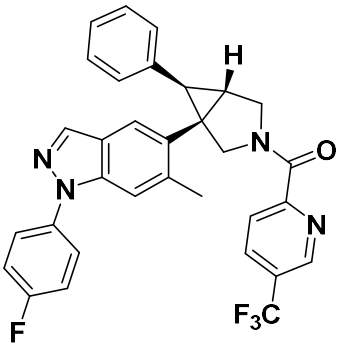


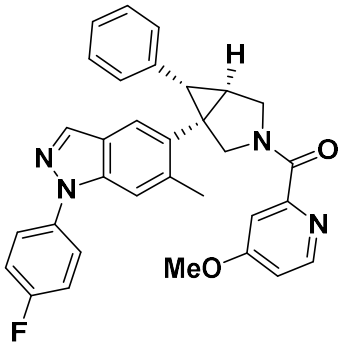
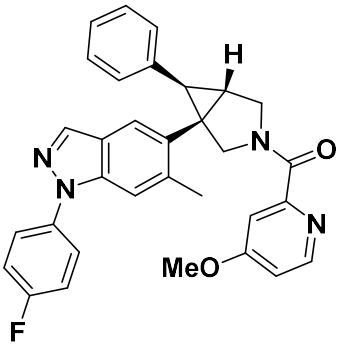
Or

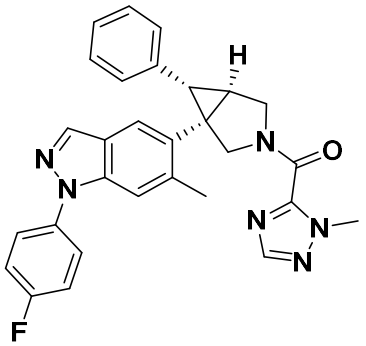
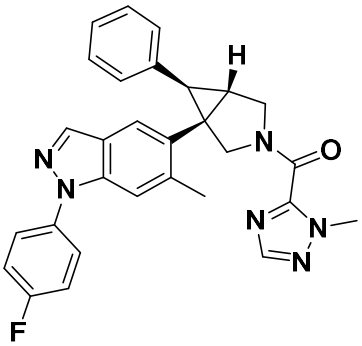


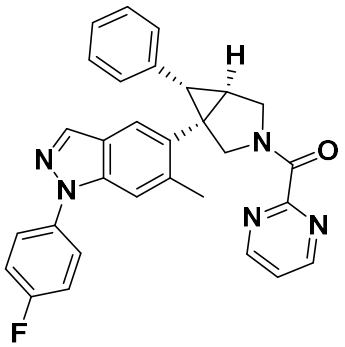
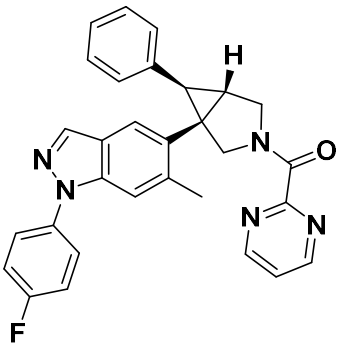
;

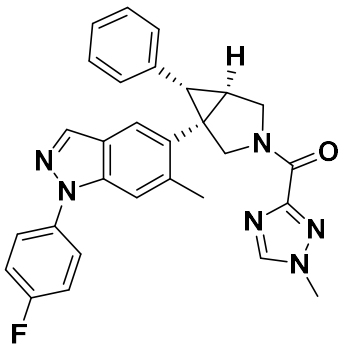
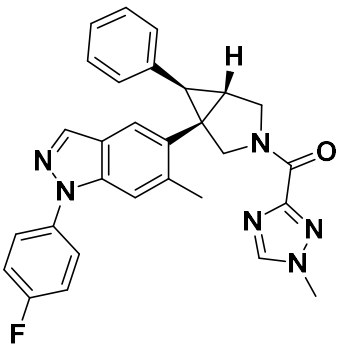

Or

;

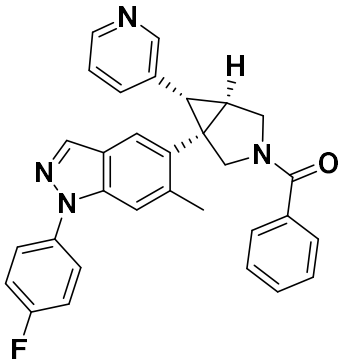
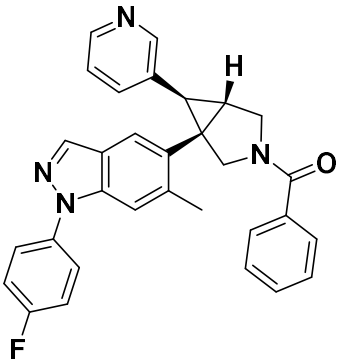

Or

;

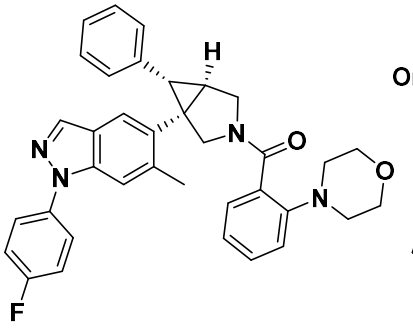
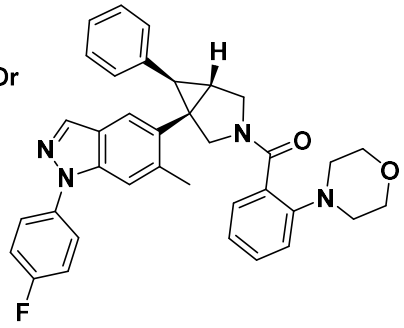

Or

;

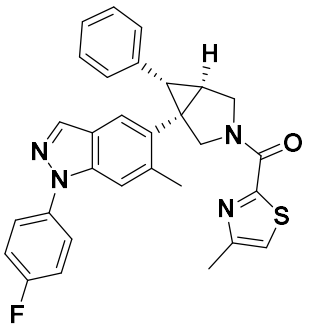
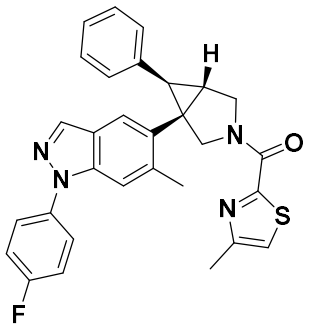

Or

;

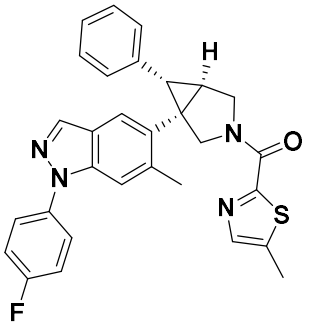
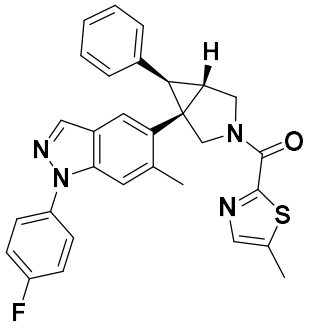

Or

;

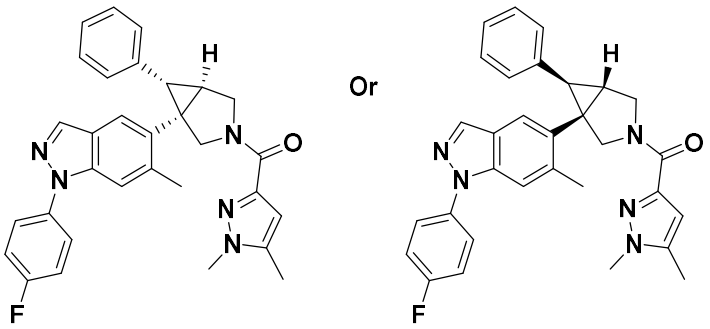

Or

;

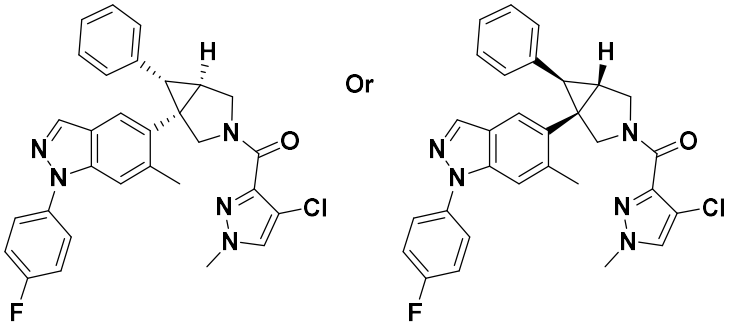


;

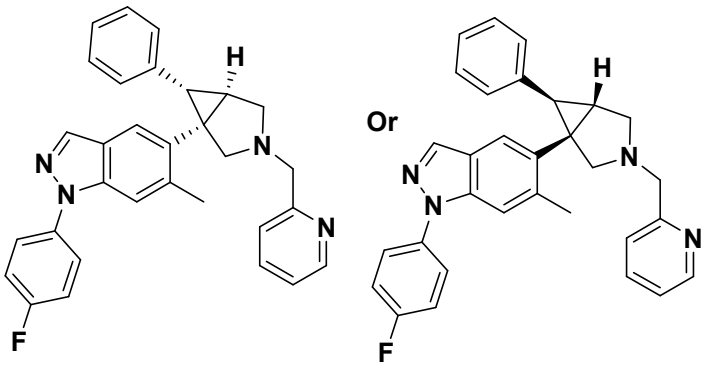

Or

;

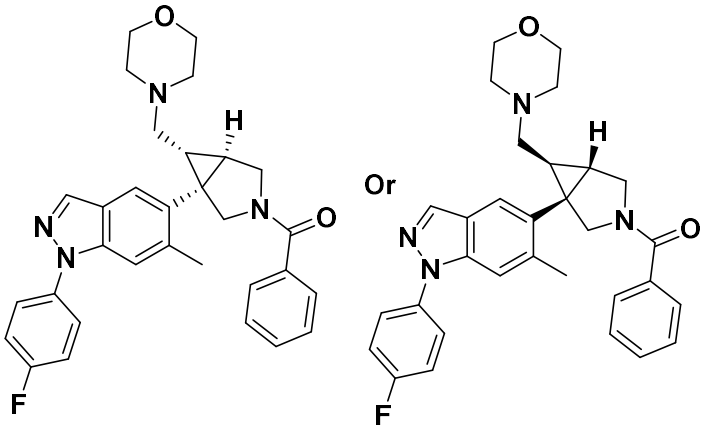

Or

;

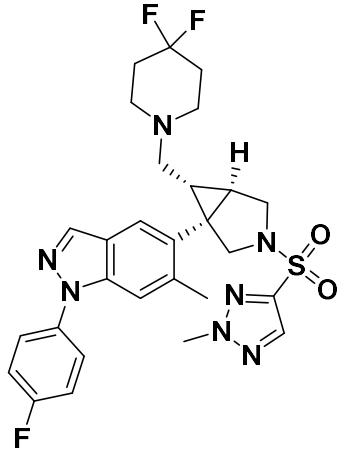
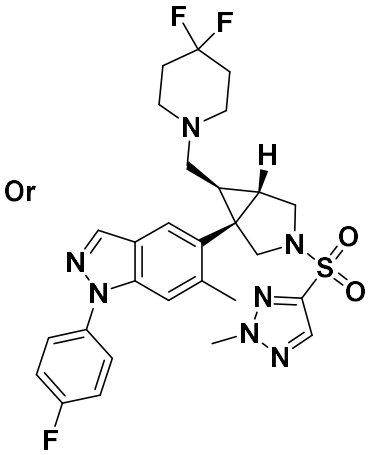

Or

;

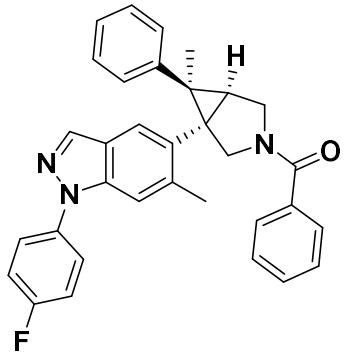
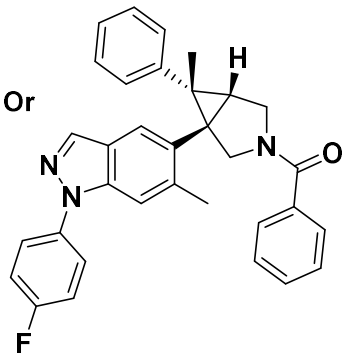

Or
;

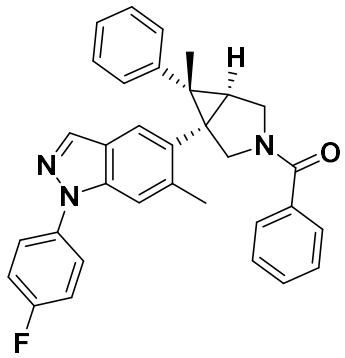
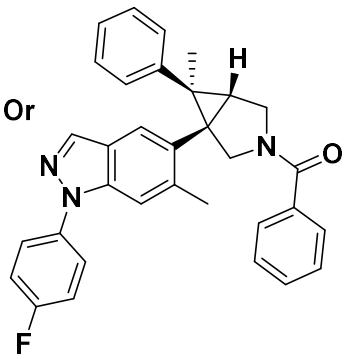

Or
;

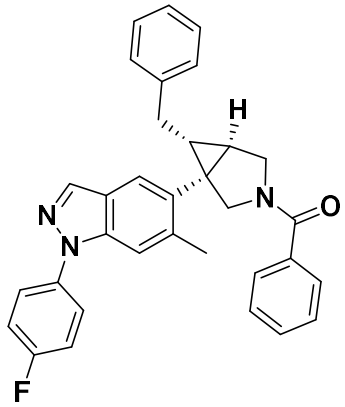
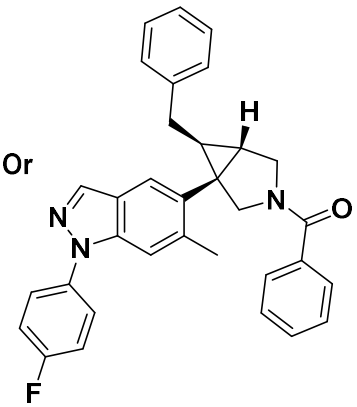

Or
;

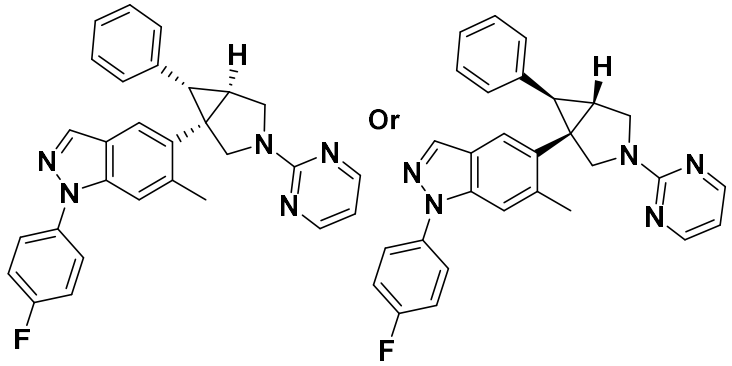

Or
;



Or ;

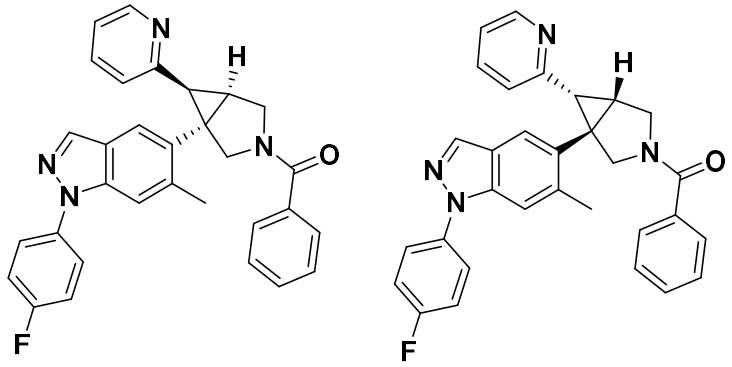


Or ;



Or ;



Or ;

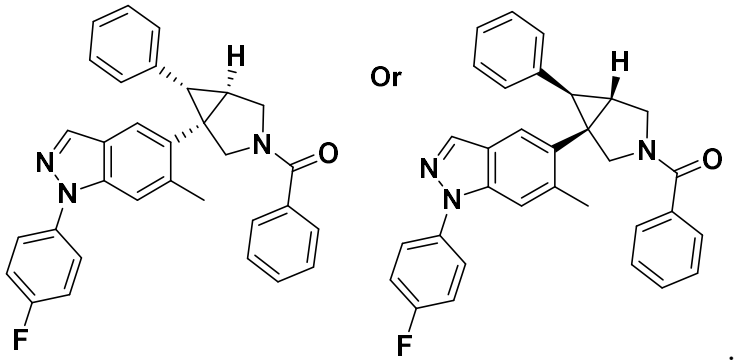


; or



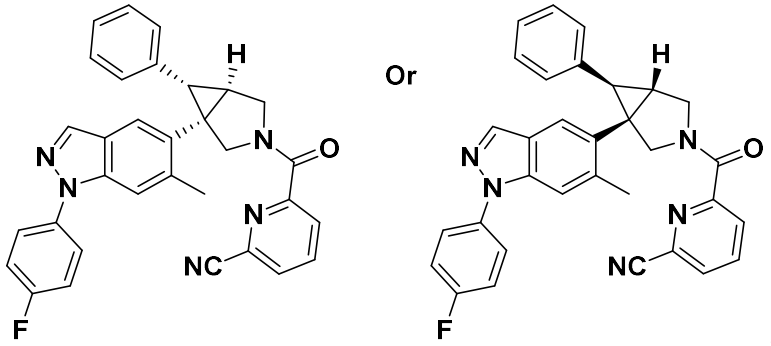
.

Claim 16. The compound of any one of claims 1 to 10, or 15, or a pharmaceutically acceptable salt thereof, having the structure:



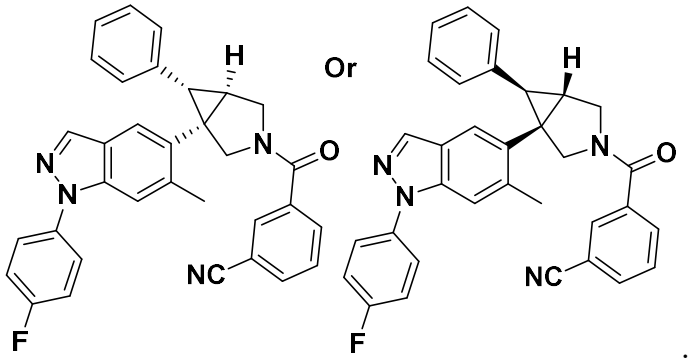
.

Claim 17. The compound of any one of claims 1 to 10, or 15, or a pharmaceutically acceptable salt thereof, having the structure:



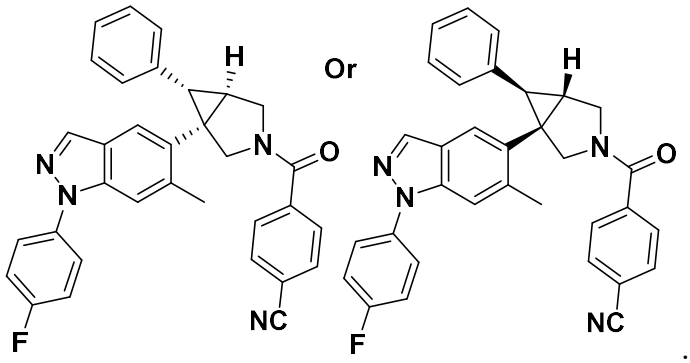
.

Claim 18. The compound of any one of claims 1 to 10, or 15, or a pharmaceutically acceptable salt thereof, having the structure:



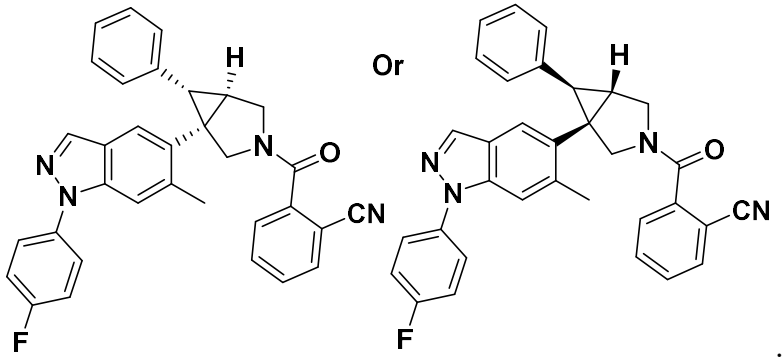
.

19. The compound of any one of claims 1 to 10, or 15, or a pharmaceutically acceptable salt thereof, having the structure:



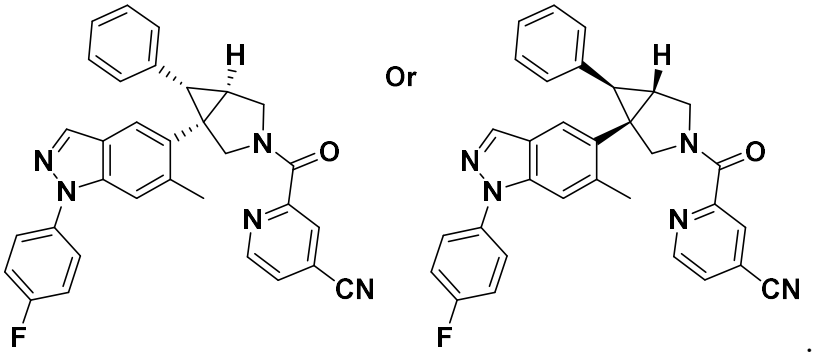
.

Claim 20. The compound of any one of claims 1 to 10, or 15, or a pharmaceutically acceptable salt thereof, having the structure:

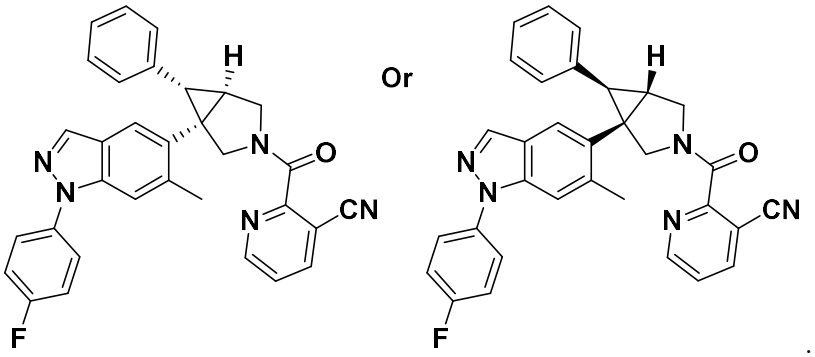


.

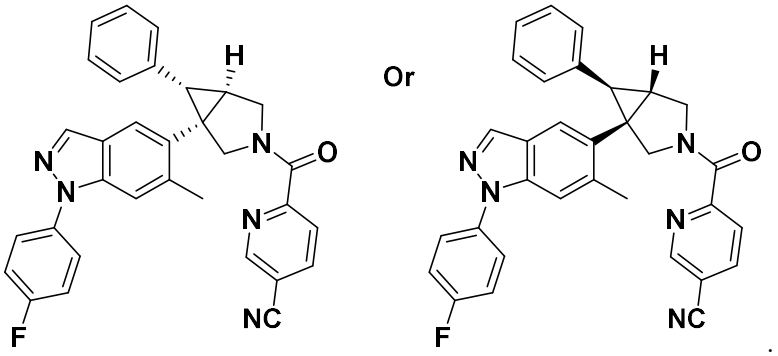
Claim 21. The compound of any one of claims 1 to 10, or 15, or a pharmaceutically acceptable salt thereof, having the structure:



Claim 22. The compound of any one of claims 1 to 10, or 15, or a pharmaceutically acceptable salt thereof, having the structure:



Claim 23. The compound of any one of claims 1 to 10, or 15, or a pharmaceutically acceptable salt thereof, having the structure:



Claim 24. A pharmaceutical composition comprising a compound of any one of claims 1 to 23, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

Claim 25. A compound of any one of claims 1 to 23, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 24, for

use in a method of treating a disorder or condition through modulating or antagonising a glucocorticoid receptor.

Claim 26. The compound or pharmaceutical composition for use of claim 25, wherein the disorder or condition is selected from the group consisting of Alzheimer's disease, amyotrophic lateral sclerosis (ALS), antipsychotic induced weight gain, cancer, Cushing Disease, Cushing's Syndrome, major psychotic depression, nonalcoholic steatohepatitis, and obesity.

Claim 27. Use of a compound of any one of claims 1 to 23, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 24, in the manufacture of a medicament for treating a disorder or condition through modulating or antagonizing a glucocorticoid receptor.

Claim 28. The use of claim 27, wherein the disorder or condition is selected from the group consisting of Alzheimer's disease, amyotrophic lateral sclerosis (ALS), antipsychotic induced weight gain, cancer, Cushing Disease, Cushing's Syndrome, major psychotic depression, nonalcoholic steatohepatitis, and obesity.