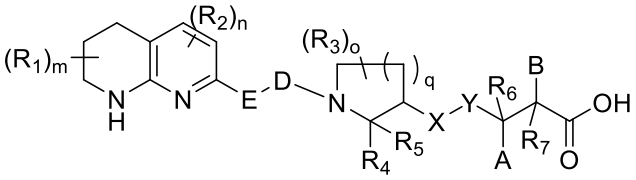
to a diverse set of human diseases, including. for example, platelet disorders, atherosclerosis, cancer, osteoporosis, fibrosis, diabetic neuropathy of the kidney, macular degeneration and various autoimmune and chronic inflammation diseases.

[0005] Accordingly, αVβ6 and αVβ1 integrin inhibitors have been extensively investigated but despite immense effort, therapeutic success has been elusive. Accordingly, there is a need for αVβ6 and αVβ1 integrin inhibitors, which in some examples are orally deliverable and may, for example, treat and/or prevent platelet disorders, atherosclerosis, cancer, osteoporosis, fibrosis, diabetic neuropathy of the kidney, macular degeneration and various autoimmune and chronic inflammation diseases.

BRIEF SUMMARY

[0005a] In an aspect of the present disclosure, there is provided a compound of Formula (I):



(I)

or pharmaceutically acceptable salts, hydrates or solvates thereof wherein:

each R_1 is independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl or substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted heteroalkenyl, heteroalkynyl, substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, heteroarylalkynyl, substituted heteroarylalkynyl,

halo, $-C(O)NR_8R_9$, $-C(O)OR_{10}$, $-NR_{11}C(O)OR_{12}$, $-NR_{13}C(O)OR_{14}$, $-OC(O)OR_{15}$, -CN, $-CF_3$, $-NR_{16}SO_2R_{17}$ or $-OR_{18}$;

m is 0, 1, 2 or 3;

each R_2 is independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl, substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted

heteroalkenyl, heteroalkynyl, substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, heteroarylalkynyl, substituted heteroarylalkynyl,
halo, $-C(O)NR_{19}R_{20}$, $-C(O)OR_{21}$, $-NR_{22}C(O)OR_{23}$, $-NR_{24}C(O)OR_{25}$, $-OC(O)OR_{26}$, -CN, $-CF_3$, $-NR_{27}SO_2R_{28}$ or $-OR_{29}$;
n is 0, 1 or 2;
each R_3 is independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl, substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted heteroalkenyl, heteroalkynyl, substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, heteroarylalkynyl, substituted heteroarylalkynyl,
halo, $-C(O)NR_{30}R_{31}$, $-C(O)OR_{32}$, $-NR_{33}C(O)OR_{34}$, $-NR_{35}C(O)OR_{36}$, $-OC(O)OR_{37}$, -CN, $-CF_3$, $-NR_{38}SO_2R_{39}$ or $-OR_{40}$;
q is 0, 1, 2 or 3;
o is 0, 1 or 2 when q is 0;
o is 0, 1, 2 or 3 when q is 1;
o is 0, 1, 2, 3 or 4 when q is 2;
o is 0, 1, 2, 3, 4 or 5 when q is 3;
R_4 is hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl, substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted heteroalkenyl, heteroalkynyl, substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, heteroarylalkynyl, substituted heteroarylalkynyl, -F, $-C(O)NR_{41}R_{42}$, $-C(O)R_{43}$, $-C(O)OR_{44}$, -CN, $-CF_3$ or R_4 and R_5 together with the atom to which they are bonded form a C_4-C_8 cycloalkyl ring;
E is $-CH_2-$ or $-CH_2Z-$;
Z is $-NR_{46}-$, -S-, $-SO_2-$ or -O-;

D is -$(CH_2)_2$-, -$(CH_2)_3$-, -CH=CHCH_2-, -C(O)-, -C≡CCH_2-, phenyl, cyclohexyl or cyclopentyl when E is -CH_2-; D is -$(CH_2)_2$-, -$(CH_2)_3$-, -C(O)-, phenyl, cyclohexyl or cyclopentyl when Z is NR_{45} or -O-; D is -$(CH_2)_2$-, -$(CH_2)_3$-, phenyl, cyclohexyl or cyclopentyl when Z is -SO_2- or -S-;

X-Y

is -C(O)NR_{46}-, -NR_{47}C(O)-, -C(O)O-, -CH_2CH_2-, -CH=CH-, -C≡C-, -$NR_{48}CH_2$-, -CH_2NR_{49}-, -O-CH_2-, -CH_2-O-, -SO_2NR_{50}-, -$NR_{51}SO_2$- or cyclopropyl;

A is hydrogen, -OR_{52}, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl, substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted heteroalkenyl, heteroalkynyl, substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, heteroarylalkynyl, substituted heteroarylalkynyl or halo;

B is hydrogen, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl, substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted heteroalkenyl, heteroalkynyl, substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, heteroarylalkynyl, substituted heteroarylalkynyl, halo, -$NR_{53}R_{54}$, -O-R_{55}, -S-R_{56} or -SO_2-R_{57};

R_8-R_{53} and R_{58}-R_{64} are independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl, substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted heteroalkenyl, heteroalkynyl, substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, heteroarylalkynyl or substituted heteroarylalkynyl;

R_{54} is alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl, substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted heteroalkenyl, heteroalkynyl,

substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, heteroarylalkynyl, substituted heteroarylalkynyl, -C(O)R_{58}, -C(O)OR_{59}, -C(O)$NR_{60}R_{61}$, or -SO_2R_{62};

R_{55}-R_{57} are alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl, substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted heteroalkenyl, heteroalkynyl, substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, heteroarylalkynyl or substituted heteroarylalkynyl;

R_5 is hydrogen or -F;

R_6 is hydrogen, -F or -OR_{63}; and

R_7 is hydrogen, -F or -OR_{64};

provided that R_5 is hydrogen when R_4 is -C(O)$NR_{41}R_{42}$, -C(O)R_{43}, -C(O)OR_{44} or -CN;

provided that A is not hydrogen, halo or -OR_{52} when B is hydrogen or halo;

provided that B is not hydrogen or halo when A is hydrogen, halo or -OR_{52};

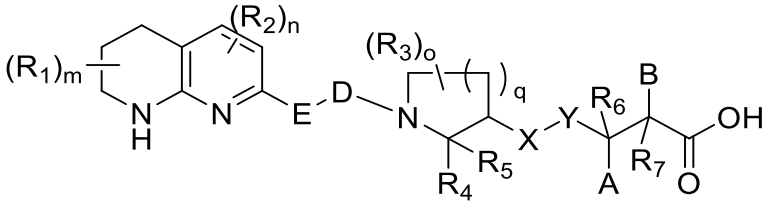
provided that R_7 is hydrogen when B is halo, -$NR_{53}R_{54}$, -O-R_{55}, -S-R_{56} or -SO_2R_{57};

provided that R_6 is -OR_{63} only when X-Y are -CH_2CH_2-, -CH=CH-, -C≡C- or cyclopropyl;

provided that A is not -OR_{52} when R_6 is -OR_{63}; and

provided that A is not -Cl, -Br or -I when R_6 is -F.

[0005b] In another aspect of the present disclosure, there is provided a compound of Formula (Ia):



(Ia)

or pharmaceutically acceptable salts thereof, wherein:

q is 1, 2 or 3;

R^1 and R^3 are each independently selected at each occurrence from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-C(O)OR^{11}$, =O, =S, and $-CN$;

m is selected from 0, 1, 2, 3, 4, 5, and 6;

o is selected from 0, 1, 2, 3, 4, 5, 6, 7, and 8;

R^2 is independently selected at each occurrence from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{12}$, $-SR^{12}$, $-N(R^{12})_2$, $-CN$, and $-NO_2$;

n is 0, 1 or 2;

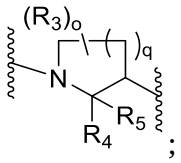
R^4 and R^5 are each independently selected from hydrogen, halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{13}$, $-SR^{13}$, $-N(R^{13})_2$, and $-CN$; or R^4 and R^5 are taken together to form a double bonded substituent selected from =O, =S and $=N(R^{13})$;

D is selected from a bond, $-C(O)-$, $-C\equiv CCH_2-$, and $-CH=CHCH_2-$;

E is selected from C_{1-4} alkylene and $-(CH_2)Z-$,

wherein Z is selected from $-NH-$, $-S-$, $-SO_2-$, and $-O-$;

X-Y is selected from: $^{\lambda}-C(O)N(R^{14})-$, $^{\lambda}-N(R^{14})C(O)-$, $^{\lambda}-N(R^{14})C(O)C(R^{15})_2-$, $^{\lambda}-C(O)O-$, $^{\lambda}-C(R^{15})_2C(R^{15})_2-$, $^{\lambda}-CH=CH-$, $^{\lambda}-C\equiv C-$, $^{\lambda}-N(R^{14})C(R^{15})_2-$, $^{\lambda}-C(R^{15})_2N(R^{14})-$, $^{\lambda}-O-$, $^{\lambda}-OC(R^{15})_2-$, $^{\lambda}-C(R^{15})_2O-$, $^{\lambda}-SO_2N(R^{14})-$, and $^{\lambda}-N(R^{14})SO_2-$;

wherein $^{\lambda}$ denotes the attachment of X-Y to 

;

R^6 and R^7 are each independently selected at each occurrence from:

hydrogen, halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, and $-CN$;

A is selected from (i) and (ii):

(i) hydrogen, halogen, and $-CN$, or A and R^6 come together to form a C_{3-6} carbocycle or 3- to 6-membered heterocycle;

(ii) $-OR^{17}$, $-SR^{17}$, $-N(R^{17})_2$, $-N(R^{17})C(O)R^{17}$, $-N(R^{17})C(O)OR^{17}$, $-N(R^{17})C(O)N(R^{17})_2$, $-N(R^{17})C(S)N(R^{17})_2$, $-N(R^{17})S(O)_2(R^{17})$, $-C(O)R^{17}$, $-C(O)OR^{17}$, $-OC(O)R^{17}$, $-OC(O)N(R^{17})_2$, $-C(O)N(R^{17})_2$, $-S(O)R^{17}$, $-S(O)_2R^{17}$, and $-S(O)_2N(R^{17})_2$;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{17}$, $-SR^{17}$, $-N(R^{17})_2$, $-C(O)R^{17}$, $-C(O)OR^{17}$, $-OC(O)R^{17}$, $-OC(O)N(R^{17})_2$, $-C(O)N(R^{17})_2$, $-N(R^{17})C(O)R^{17}$, $-N(R^{17})C(O)OR^{17}$, $-N(R^{17})C(O)N(R^{17})_2$, $-N(R^{17})C(S)N(R^{17})_2$, $-N(R^{17})S(O)_2(R^{17})$, $-S(O)R^{17}$, $-S(O)_2R^{17}$, $-S(O)_2N(R^{17})_2$, $-NO_2$, =O, =S, $=N(R^{17})$, $-N_3$, and $-CN$, C_{3-10} carbocycle, and 3- to 10-membered heterocycle,

wherein the C_{3-10} carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more substituents independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^{17}$, $-SR^{17}$, $-N(R^{17})_2$, $-C(O)R^{17}$, $-C(O)OR^{17}$, $-OC(O)R^{17}$, $-OC(O)N(R^{17})_2$,

$-C(O)N(R^{17})_2$, $-N(R^{17})C(O)R^{17}$, $-N(R^{17})C(O)OR^{17}$, $-N(R^{17})C(O)N(R^{17})_2$, $-N(R^{17})C(S)N(R^{17})_2$, $-N(R^{17})S(O)_2(R^{17})$, $-S(O)R^{17}$, $-S(O)_2R^{17}$, $-S(O)_2N(R^{17})_2$, $-NO_2$, =O, =S, $=N(R^{17})$, $-N_3$, and −CN; and

C_{3-12} carbocycle and 3- to 12-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{17}$, $-SR^{17}$, $-N(R^{17})_2$, $-C(O)R^{17}$, $-C(O)OR^{17}$, $-OC(O)R^{17}$, $-OC(O)N(R^{17})_2$, $-C(O)N(R^{17})_2$, $-N(R^{17})C(O)R^{17}$, $-N(R^{17})C(O)OR^{17}$, $-N(R^{17})C(O)N(R^{17})_2$, $-N(R^{17})C(S)N(R^{17})_2$, $-N(R^{17})S(O)_2(R^{17})$, $-S(O)R^{17}$, $-S(O)_2R^{17}$, $-S(O)_2N(R^{17})_2$, $-NO_2$, =O, =S, $=N(R^{17})$, $-N_3$, and −CN;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, $-OR^{17}$, $-SR^{17}$, $-N(R^{17})_2$, $-C(O)R^{17}$, $-C(O)OR^{17}$, $-OC(O)R^{17}$, $-OC(O)N(R^{17})_2$, $-C(O)N(R^{17})_2$, $-N(R^{17})C(O)R^{17}$, $-N(R^{17})C(O)OR^{17}$, $-N(R^{17})C(O)N(R^{17})_2$, $-N(R^{17})C(S)N(R^{17})_2$, $-N(R^{17})S(O)_2(R^{17})$, $-S(O)R^{17}$, $-S(O)_2R^{17}$, $-S(O)_2N(R^{17})_2$, $-NO_2$, =O, =S, $=N(R^{17})$, $-N_3$, and −CN; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, and =O;

B is selected from (I) when A is selected from (ii), or

B is selected from (II) when A is selected from (i):

(I) hydrogen, halogen, and -CN, or B and R^7 are taken together to form a C_{3-6} carbocycle or a 3- to 6-membered heterocycle;

(II) $-OR^{18}$, $-SR^{18}$, $-N(R^{18})_2$, $-C(O)R^{18}$, $-C(O)OR^{18}$, $-OC(O)R^{18}$, $-OC(O)N(R^{18})_2$, $-C(O)N(R^{18})_2$, $-N(R^{18})C(O)R^{18}$, $-N(R^{18})C(O)OR^{18}$, $-N(R^{18})C(O)N(R^{18})_2$, $-N(R^{18})C(S)N(R^{18})_2$, $-N(R^{18})S(O)_2(R^{18})$, $-S(O)R^{18}$, $-S(O)_2R^{18}$, and $-S(O)_2N(R^{18})_2$;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{18}$, $-SR^{18}$, $-N(R^{18})_2$, $-C(O)R^{18}$, $-C(O)OR^{18}$, $-OC(O)R^{18}$, $-OC(O)N(R^{18})_2$, $-C(O)N(R^{18})_2$, $-N(R^{18})C(O)R^{18}$, $-N(R^{18})C(O)OR^{18}$, $-N(R^{18})C(O)N(R^{18})_2$, $-N(R^{18})C(S)N(R^{18})_2$, $-N(R^{18})S(O)_2(R^{18})$, $-S(O)R^{18}$, $-S(O)_2R^{18}$, $-S(O)_2N(R^{18})_2$, $-NO_2$, =O, =S, $=N(R^{18})$, $-N_3$,−CN, C_{3-10} carbocycle and 3- to 10-membered heterocycle,

wherein the C_{3-10} carbocycle and 3- to 10-membered heterocycle are optionally substituted with one or more substituents independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^{18}$, $-SR^{18}$, $-N(R^{18})_2$, $-C(O)R^{18}$, $-C(O)OR^{18}$, $-OC(O)R^{18}$, $-OC(O)N(R^{18})_2$, $-C(O)N(R^{18})_2$, $-N(R^{18})C(O)R^{18}$, $-N(R^{18})C(O)OR^{18}$, $-N(R^{18})C(O)N(R^{18})_2$, $-N(R^{18})C(S)N(R^{18})_2$, $-N(R^{18})S(O)_2(R^{18})$, $-S(O)R^{18}$, $-S(O)_2R^{18}$, $-S(O)_2N(R^{18})_2$, $-NO_2$, =O, =S, $=N(R^{18})$, $-N_3$, and −CN; and

C_{3-12} carbocycle and 3- to 12-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{18}$, $-SR^{18}$, $-N(R^{18})_2$, $-C(O)R^{18}$, $-C(O)OR^{18}$, $-OC(O)R^{18}$, $-OC(O)N(R^{18})_2$, $-C(O)N(R^{18})_2$, $-N(R^{18})C(O)R^{18}$, $-N(R^{18})C(O)OR^{18}$, $-N(R^{18})C(O)N(R^{18})_2$, $-N(R^{18})C(S)N(R^{18})_2$, $-N(R^{18})S(O)_2(R^{18})$, $-S(O)R^{18}$, $-S(O)_2R^{18}$, $-S(O)_2N(R^{18})_2$, $-NO_2$, =O, =S, $=N(R^{18})$, $-N_3$, and −CN;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{18}$, $-SR^{18}$, $-N(R^{18})_2$, $-C(O)R^{18}$, $-C(O)OR^{18}$, $-OC(O)R^{18}$, $-OC(O)N(R^{18})_2$, $-C(O)N(R^{18})_2$, $-N(R^{18})C(O)R^{18}$, $-N(R^{18})C(O)OR^{18}$, $-N(R^{18})C(O)N(R^{18})_2$, $-N(R^{18})C(S)N(R^{18})_2$, $-N(R^{18})S(O)_2(R^{18})$, $-S(O)R^{18}$, $-S(O)_2R^{18}$, $-S(O)_2N(R^{18})_2$, $-NO_2$, =O, =S, $=N(R^{18})$, $-N_3$,−CN, C_{3-6} carbocycle and 3- to 6-membered heterocycle,

wherein the C_{3-6} carbocycle and 3- to 6-membered heterocycle are each optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, and =O; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, and =O;

R^{11}, R^{12}, R^{13}, R^{14}, and R^{16} are each independently selected at each occurrence from hydrogen, C_{1-4} alkyl, and C_{1-4} haloalkyl;

R^{15} is independently selected at each occurrence from hydrogen, halogen, C_{1-4} alkyl, and C_{1-4} haloalkyl;

R^{17} is independently selected at each occurrence from:

hydrogen;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{21}$, $-SR^{21}$, $-N(R^{21})_2$, $-C(O)R^{21}$, $-C(O)OR^{21}$, $-OC(O)R^{21}$, $-OC(O)N(R^{21})_2$, $-C(O)N(R^{21})_2$, $-N(R^{21})C(O)R^{21}$, $-NO_2$, =O, =S, $=N(R^{21})$, $-N_3$, and −CN; and

C_{3-6} carbocycle and 3- to 6-membered heterocycle, any of which are optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{21}$, $-SR^{21}$, $-N(R^{21})_2$, $-C(O)R^{21}$, $-C(O)OR^{21}$, $-OC(O)R^{21}$, $-OC(O)N(R^{21})_2$, $-C(O)N(R^{21})_2$, $-N(R^{21})C(O)R^{21}$, $-N(R^{21})C(O)OR^{21}$, $-N(R^{21})C(O)N(R^{21})_2$, $-N(R^{21})C(S)N(R^{21})_2$, $-N(R^{21})S(O)_2(R^{21})$, $-S(O)R^{21}$, $-S(O)_2R^{21}$, $-S(O)_2N(R^{21})_2$, $-NO_2$, =O, =S, $=N(R^{21})$, $-N_3$, and −CN;

R^{18} is independently selected at each occurrence from:

hydrogen;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{22}$, $-SR^{22}$, $-N(R^{22})_2$, $-C(O)R^{22}$, $-C(O)OR^{22}$, $-OC(O)R^{22}$, $-OC(O)N(R^{22})_2$, $-C(O)N(R^{22})_2$, $-N(R^{22})C(O)R^{22}$, $-NO_2$, =O, =S, $=N(R^{22})$, $-N_3$, −CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle,

wherein the C_{3-10} carbocycle and 3- to 10-membered heterocycle each are optionally substituted with one or more substituents independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^{22}$, $-SR^{22}$, and $-N(R^{22})_2$; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^{22}$, $-SR^{22}$, $-N(R^{22})_2$, $-C(O)R^{22}$, $-C(O)OR^{22}$, $-OC(O)R^{22}$, $-OC(O)N(R^{22})_2$, $-C(O)N(R^{22})_2$, $-N(R^{22})C(O)R^{22}$, $-N(R^{22})C(O)OR^{22}$, $-N(R^{22})C(O)N(R^{22})_2$, $-N(R^{22})C(S)N(R^{22})_2$, $-N(R^{22})S(O)_2(R^{22})$, $-S(O)R^{22}$, $-S(O)_2R^{22}$, $-S(O)_2N(R^{22})_2$, $-NO_2$, =O, =S, $=N(R^{22})$, $-N_3$,−CN, C_{3-6} carbocycle, and 3- to 6-membered heterocycle;

wherein the C_{3-6} carbocycle and 3- to 6-membered heterocycle are each optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, and C_{1-4} haloalkyl;

R^{21} and R^{22} are each independently selected at each occurrence from:

hydrogen;

C_{1-4} alkyl optionally substituted with one or more substituents independently selected from halogen, hydroxyl, C_{3-6} carbocycle, and 3- to 6-membered heterocycle, wherein each C_{3-6} carbocycle and 3- to 6-membered heterocycle is optionally substituted

with one or more substituents independently selected from C_{1-4} alkyl, $-N(R^{23})_2$, and $-C(O)N(R^{23})_2$; and

C_{3-6} carbocycle and 3- to 12-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, and =O; and

R^{23} is independently selected at each occurrence from hydrogen and C_{1-4} alkyl.

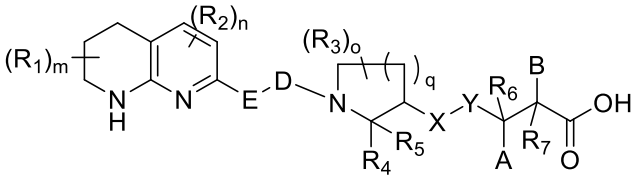
[0005c] In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising pharmaceutically acceptable excipient and a compound or salt of any one disclosed herein.

[0005d] In another aspect of the present disclosure, there is provided a compound or salt disclosed herein or a pharmaceutical composition disclosed herein, for use in therapy.

[0005e] In a further aspect of the present disclosure, there is provided a use of a compound or salt disclosed herein or a pharmaceutical composition disclosed herein, in the manufacture of a medicament for modulating an alpha V integrin in a subject in need thereof.

[0005f] In another aspect of the present disclosure, there is provided a use of a compound or salt disclosed herein or a pharmaceutical composition disclosed herein, in the manufacture of a medicament for treating a disease or condition in a subject in need thereof.

[0006] In one example, provided herein is a compound of Formula (I) which satisfies this and other needs:



(I) (I);

or pharmaceutically acceptable salts, hydrates or solvates thereof wherein:

each R_1 is independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl or substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted heteroalkenyl, heteroalkynyl, substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, heteroarylalkynyl, substituted heteroarylalkynyl,

halo, $-C(O)NR_8R_9$, $-C(O)OR_{10}$, $-NR_{11}C(O)OR_{12}$, $-NR_{13}C(O)OR_{14}$, $-OC(O)OR_{15}$, $-CN$, $-CF_3$, $-NR_{16}SO_2R_{17}$ or $-OR_{18}$; m is 0, 1, 2 or 3; each R_2 is independently hydrogen, alkyl, substituted alkyl,

alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl, substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted heteroalkenyl, heteroalkynyl, substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl,

hydrogen or halo when A is hydrogen, halo or -$OR_{52;}$ provided that R_7 is hydrogen when B is halo, -$NR_{53}R_{54}$, -O-R_{55}, -S-R_{56} or -SO_2R_{57}; provided that R_6 is -OR_{63} only when X-Y are -CH_2CH_2-, -CH=CH-, -C≡C- or cyclopropyl; provided that A is not -OR_{52} when R_6 is -OR_{63}; and provided that A is not -Cl, -Br or -I when R_6 is -F.

[0007] In another example, derivatives, including salts, esters, enol ethers, enol esters, solvates, hydrates, metabolites and prodrugs of the compounds of Formula (I) described herein are provided. Further provided are pharmaceutical compositions which include the compounds of Formula (I) provided herein and a pharmaceutically acceptable vehicle.

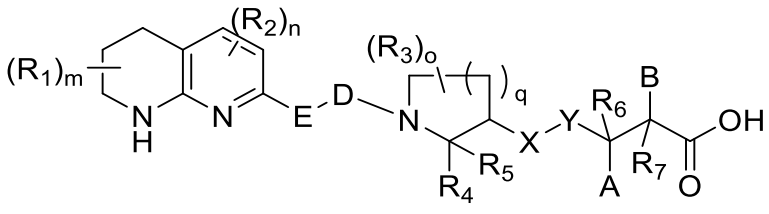
[0008] Methods of treating, preventing, or ameliorating symptoms of medical disorders such as, for example, platelet disorders, atherosclerosis, cancer, osteoporosis, fibrosis, diabetic neuropathy of the kidney, macular degeneration and various autoimmune and chronic inflammation diseases are provided herein. In practicing the methods, therapeutically effective amounts of the compounds of Formula (I) or pharmaceutical compositions thereof are administered to the patient with the disorder or condition.

[0009] Methods for inhibiting αVβ6 integrin in a patient are described herein. In practicing the methods, therapeutically effective amounts of the compounds of Formula (I) or pharmaceutical compositions thereof are administered to the patient.

[0010] Methods for inhibiting αVβ1 integrin in a patient are described herein. In practicing the methods, therapeutically effective amounts of the compounds of Formula (I) or pharmaceutical compositions thereof are administered to the patient.

[0011] Methods for inhibiting TGFβ activation in a cell are provided herein. In practicing the methods, effective amounts of the compounds or Formula (I) of pharmaceutical compositions thereof are administered to the cell.

[0012] In one example, provided herein is a compound of Formula (Ia) which satisfies this and other needs:



(Ia)

or pharmaceutically acceptable salts thereof, wherein:

q is 1, 2 or 3;

R^1 and R^3 are each independently selected at each occurrence from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-C(O)OR^{11}$, =O, =S, and −CN;

m is selected from 0, 1, 2, 3, 4, 5, and 6;

C_{1-4} alkyl optionally substituted with one or more substituents independently selected from halogen, hydroxyl, C_{3-6} carbocycle, and 3- to 6-membered heterocycle, wherein each C_{3-6} carbocycle and 3- to 6-membered heterocycle is optionally substituted with one or more substituents independently selected from C_{1-4} alkyl, $-N(R^{23})_2$, and $-C(O)N(R^{23})_2$; and

C_{3-6} carbocycle and 3- to 12-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, and =O; and

R^{23} is independently selected at each occurrence from hydrogen and C_{1-4} alkyl.

[0013] In one example, the present disclosure provides a pharmaceutical composition comprising pharmaceutically acceptable excipient and a compound or salt of Formula (Ia).

[0014] In one example, the present disclosure provides a method of modulating an alpha V integrin in a subject in need thereof, comprising administering to the subject a compound or salt of Formula (Ia) or a pharmaceutical composition of Formula (Ia).

[0015] In some examples, the alpha V integrin is an alpha V beta 1 integrin.

[0016] In some examples, the alpha V integrin is an alpha V beta 6 integrin.

[0017] In one example, the present disclosure provides a method of treating a disease or condition comprising administering to a subject in need thereof a compound or salt of Formula (Ia) or a pharmaceutical composition comprising a compound or salt of Formula (Ia).

[0018] In some examples, the disease or condition is selected from: idiopathic pulmonary fibrosis, systemic lupus erythematosus associated interstitial lung disease, rheumatoid arthritis, diabetic nephropathy, focal segmental glomerulosclerosis, chronic kidney disease, nonalcoholic steatohepatitis, primary biliary cholangitis, primary sclerosing cholangitis, solid tumors, hematological tumors, organ transplant, Alport syndrome, interstitial lung disease, radiation-induced fibrosis, bleomycin-induced fibrosis, asbestos-induced fibrosis, flu-induced fibrosis, coagulation-induced fibrosis, vascular injury-induced fibrosis, aortic stenosis, and cardiac fibrosis.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019] FIG. 1 illustrates Scheme 1 which describes the synthesis of intermediate 10.

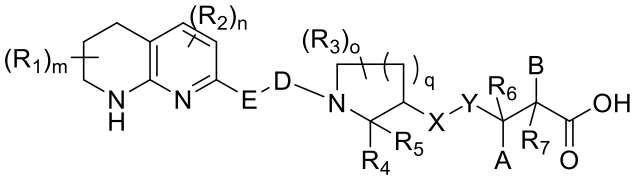
[0020] FIG. 2 illustrates Scheme 2 which describes a synthesis of compounds of Formula (VII).

[0021] FIG. 3 illustrates Scheme 4 which describes another synthesis of compounds of Formula (VII).

CLAIMS

What is claimed is:

1. A compound of Formula (I):



(I)

or pharmaceutically acceptable salts, hydrates or solvates thereof wherein:

each R_1 is independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl or substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted heteroalkenyl, heteroalkynyl, substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, heteroarylalkynyl, substituted heteroarylalkynyl,

halo, $-C(O)NR_8R_9$, $-C(O)OR_{10}$, $-NR_{11}C(O)OR_{12}$, $-NR_{13}C(O)OR_{14}$, $-OC(O)OR_{15}$, -CN, $-CF_3$, $-NR_{16}SO_2R_{17}$ or $-OR_{18}$;

m is 0, 1, 2 or 3;

each R_2 is independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl, substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted heteroalkenyl, heteroalkynyl, substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, heteroarylalkynyl, substituted heteroarylalkynyl,

halo, $-C(O)NR_{19}R_{20}$, $-C(O)OR_{21}$, $-NR_{22}C(O)OR_{23}$, $-NR_{24}C(O)OR_{25}$, $-OC(O)OR_{26}$, -CN, $-CF_3$, $-NR_{27}SO_2R_{28}$ or $-OR_{29}$;

n is 0, 1 or 2;

each R_3 is independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl,

substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl, substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted heteroalkenyl, heteroalkynyl, substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, heteroarylalkynyl, substituted heteroarylalkynyl,
halo, $-C(O)NR_{30}R_{31}$, $-C(O)OR_{32}$, $-NR_{33}C(O)OR_{34}$, $-NR_{35}C(O)OR_{36}$, $-OC(O)OR_{37}$, -CN, $-CF_3$, $-NR_{38}SO_2R_{39}$ or $-OR_{40}$;
q is 0, 1, 2 or 3;
o is 0, 1 or 2 when q is 0;
o is 0, 1, 2 or 3 when q is 1;
o is 0, 1, 2, 3 or 4 when q is 2;
o is 0, 1, 2, 3, 4 or 5 when q is 3;
R_4 is hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl, substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted heteroalkenyl, heteroalkynyl, substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, heteroarylalkynyl, substituted heteroarylalkynyl, -F, $-C(O)NR_{41}R_{42}$, $-C(O)R_{43}$, $-C(O)OR_{44}$, -CN, $-CF_3$ or R_4 and R_5 together with the atom to which they are bonded form a C_4-C_8 cycloalkyl ring;
E is $-CH_2-$ or $-CH_2Z-$;
Z is $-NR_{46}-$, -S-, $-SO_2-$ or -O-;
D is $-(CH_2)_2-$, $-(CH_2)_3-$, $-CH=CHCH_2-$, $-C(O)-$, $-C\equiv CCH_2-$, phenyl, cyclohexyl or cyclopentyl when E is $-CH_2-$; D is $-(CH_2)_2-$, $-(CH_2)_3-$, -C(O)-, phenyl, cyclohexyl or cyclopentyl when Z is NR_{45} or -O-; D is $-(CH_2)_2-$, $-(CH_2)_3-$, phenyl, cyclohexyl or cyclopentyl when Z is $-SO_2-$ or -S-;
X-Y
is $-C(O)NR_{46}-$, $-NR_{47}C(O)-$, $-C(O)O-$, $-CH_2CH_2-$, -CH=CH-, $-C\equiv C-$, $-NR_{48}CH_2-$, $-CH_2NR_{49}-$, $-O-CH_2-$, $-CH_2-O-$, $-SO_2NR_{50}-$, $-NR_{51}SO_2-$ or cyclopropyl;
A is hydrogen, $-OR_{52}$, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl, substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted heteroalkenyl,

heteroalkynyl, substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, heteroarylalkynyl, substituted heteroarylalkynyl or halo;

B is hydrogen, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl, substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted heteroalkenyl, heteroalkynyl, substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, heteroarylalkynyl, substituted heteroarylalkynyl, halo, $-NR_{53}R_{54}$, $-O-R_{55}$, $-S-R_{56}$ or $-SO_2-R_{57}$;

R_8-R_{53} and R_{58}-R_{64} are independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl, substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted heteroalkenyl, heteroalkynyl, substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, heteroarylalkynyl or substituted heteroarylalkynyl;

R_{54} is alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl, substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted heteroalkenyl, heteroalkynyl, substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, heteroarylalkynyl, substituted heteroarylalkynyl, $-C(O)R_{58}$, $-C(O)OR_{59}$, $-C(O)NR_{60}R_{61}$, or $-SO_2R_{62}$;

R_{55}-R_{57} are alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, arylalkynyl, substituted arylalkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl, substituted cycloheteroalkenyl, heteroalkyl, substituted heteroalkyl, heteroalkenyl, substituted heteroalkenyl, heteroalkynyl, substituted heteroalkynyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, heteroarylalkynyl or substituted heteroarylalkynyl;

R_5 is hydrogen or -F;

R_6 is hydrogen, -F or -OR_{63}; and

R_7 is hydrogen, -F or -OR_{64};

provided that R_5 is hydrogen when R_4 is -$C(O)NR_{41}R_{42}$, -$C(O)R_{43}$, -$C(O)OR_{44}$ or -CN;

provided that A is not hydrogen, halo or -OR_{52} when B is hydrogen or halo;

provided that B is not hydrogen or halo when A is hydrogen, halo or -OR_{52};

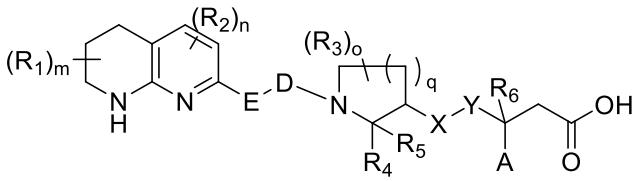
provided that R_7 is hydrogen when B is halo, -$NR_{53}R_{54}$, -O-R_{55}, -S-R_{56} or -SO_2R_{57};

provided that R_6 is -OR_{63} only when X-Y are -CH_2CH_2-, -CH=CH-, -C≡C- or cyclopropyl;

provided that A is not -OR_{52} when R_6 is -OR_{63}; and

provided that A is not -Cl, -Br or -I when R_6 is -F.

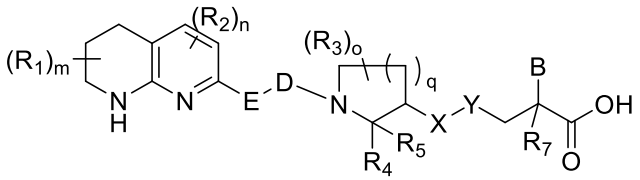
2. The compound of claim 1 of Formula (II):



(II)

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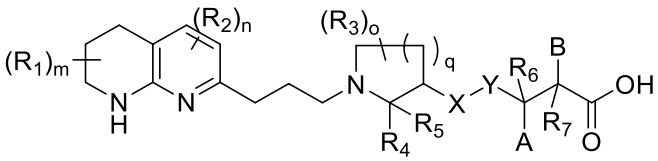
3. The compound of claim 1 of Formula (III):



(III)

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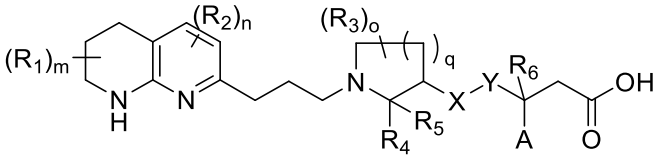
4. The compound of claim 1 of Formula (IV):



(IV)

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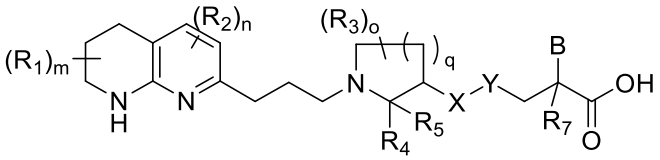
5. The compound of claim 1 of Formula (V):



(V)

.

6. The compound of claim 1 of Formula (VI):



(VI)

.

7. The compound of any one of claims 1-6, wherein each R_1 is independently alkyl, substituted alkyl, alkenyl, substituted alkenyl, phenyl, substituted phenyl, cycloalkyl, cycloheteroalkyl, heteroalkyl, -F, -C(O)NR_8R_9, -C(O)OR_{10}, -OC(O)OR_{15}, -CF_3, or -OR_{18}.

8.The compound of any one of claims 1-6, wherein each R_1 is independently (C_1-C_4) alkyl, (C_2-C_4) alkenyl, phenyl, substituted phenyl, (C_5-C_7) cycloalkyl, (C_5-C_7)cycloheteroalkyl, -F, or -CF_3.

9.The compound of any one of claims 1-6, wherein m is 0 or 1.

10.The compound of any one of claims 1-6, wherein each R_2 is independently alkyl, substituted alkyl, alkenyl, substituted alkenyl, phenyl, substituted phenyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heteroalkyl, cycloheteroalkyl, cycloheteroalkenyl, halo, -C(O)$NR_{19}R_{20}$, -C(O)OR_{21}, -NR_{22}C(O)OR_{23}, -NR_{24}C(O)OR_{25}, -OC(O)OR_{26}, -CN, -CF_3, -$NR_{27}SO_2R_{28}$ or -OR_{29}.

11. The compound of any one of claims 1-6, wherein each R_2 is independently (C_1-C_4) alkyl, (C_2-C_4) alkenyl, phenyl, substituted phenyl, (C_5-C_7) cycloalkyl, (C_5-C_7) cycloheteroalkyl, halo, C(O)$NR_{19}R_{20}$, -C(O)OR_{21}, -NR_{22}C(O)OR_{23}, -NR_{24}C(O)OR_{25}, -OC(O)OR_{26}, -CN, -CF_3, -$NR_{27}SO_2R_{28}$ or -OR_{29}.

12. The compound of any one of claims 1-6, wherein n is 0 or 1.

13. The compound of any one of claims 1-6, wherein each R_3 is independently, alkyl, substituted alkyl, alkenyl, substituted alkenyl, phenyl, substituted phenyl, cycloalkyl, heteroalkyl, cycloheteroalkyl, -F, -C(O)$NR_{30}R_{31}$, -C(O)OR_{32}, -OC(O)OR_{37}, -CF_3, or -OR_{40}.

14. The compound of any one of claims 1-6, wherein each R_3 is independently (C_1-C_4) alkyl, (C_2-C_4) alkenyl, phenyl, substituted phenyl, (C_5-C_7) cycloalkyl, (C_5-C_7) cycloheteroalkyl, -F, or -CF_3.

15. The compound of any one of claims 1-6, wherein o is 0 or 1.

16. The compound of any one of claims 1-6, wherein o is 0, 1, 2 or 3.

17. The compound of any one of claims 1-6, wherein R_4 is hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, -F, -C(O)$NR_{41}R_{42}$, -C(O)R_{43}, -C(O)OR_{44} or -CF_3.

18. The compound of any one of claims 1-6, wherein R_4 is hydrogen, (C_1-C_4) alkyl, (C_2-C_4) alkenyl, -F or -CF_3.

19. The compound of any one of claims 1-6, wherein R_8-R_{53} and R_{58}-R_{64} are independently hydrogen, alkyl, alkenyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, cycloalkyl,

substituted cycloalkyl, heteroalkyl, heteroalkenyl, heteroaryl, substituted heteroaryl, cycloheteroalkyl or substituted cycloheteroalkyl.

20. The compound of any one of claims 1-6, wherein R_8-R_{53} and R_{58}-R_{64} are independently hydrogen, (C_1-C_4) alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, cycloheteroalkyl or substituted cycloheteroalkyl.

21. The compound of any one of claims 1-6, wherein each R_1 is independently alkyl, substituted alkyl, alkenyl, substituted alkenyl, phenyl, substituted phenyl, cycloalkyl, heteroalkyl, cycloheteroalkyl, -F, -C(O)NR_8R_9, -C(O)OR_{10}, -OC(O)OR_{15}, -CF_3, or -OR_{18}, m is 0 or 1, each R_2 is independently alkyl, substituted alkyl, alkenyl, substituted alkenyl, phenyl, substituted phenyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heteroalkyl, cycloheteroalkyl,
halo, -C(O)$NR_{19}R_{20}$, -C(O)OR_{21}, -NR_{22}C(O)OR_{23}, -NR_{24}C(O)OR_{25}, -OC(O)OR_{26}, -CN, -CF_3, -$NR_{27}SO_2R_{28}$ or -OR_{29}, n is 0 or 1, each R_3 is independently, alkyl, substituted alkyl, alkenyl, substituted alkenyl, phenyl, substituted phenyl, cycloalkyl, heteroalkyl,
cycloheteroalkyl, -F, -C(O)$NR_{30}R_{31}$, -C(O)OR_{32}, -OC(O)OR_{37}, -CF_3, or -OR_{40}, o is 0, 1, 2 or 3, R_4 is hydrogen, alkyl, substituted alkyl, alkenyl, substituted
alkenyl, -F, -C(O)$NR_{41}R_{42}$, -C(O)OR_{43}, -C(O)OR_{44} or -CF_3 and R_8-R_{53} and R_{58}-R_{64} are independently hydrogen, alkyl, alkenyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, cycloalkyl, substituted cycloalkyl, heteroalkyl, heteroalkenyl, heteroaryl, substituted heteroaryl, cycloheteroalkyl or substituted cycloheteroalkyl.

22. The compound of any one of claims 1-6, wherein each R_1 is independently (C_1-C_4) alkyl, (C_2-C_4) alkenyl, phenyl, substituted phenyl, (C_5-C_7) cycloalkyl, (C_5-C_7) cycloheteroalkyl, -F, or -CF_3, m is 0 or 1, each R_2 is independently (C_1-C_4) alkyl, (C_2-C_4) alkenyl, phenyl, substituted phenyl, (C_5-C_7) cycloalkyl, (C_5-C_7) cycloheteroalkyl, halo,
C(O)$NR_{19}R_{20}$, -C(O)OR_{21}, -NR_{22}C(O)OR_{23}, -NR_{24}C(O)OR_{25}, -OC(O)OR_{26}, -CN, -CF_3, -$NR_{27}SO_2R_{28}$ or -OR_{29}, is 0 or 1, each R_3 is independently (C_1-C_4) alkyl, (C_2-C_4) alkenyl, phenyl, substituted phenyl, (C_5-C_7) cycloalkyl, (C_5-C_7) cycloheteroalkyl, -F, or -CF_3, o is 0 or 1, R_4 is hydrogen, C_1-C_4) alkyl, (C_2-C_4) alkenyl, -F or -CF_3 and R_8-R_{53} and R_{58}-R_{64} are independently hydrogen, (C_1-C_4) alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, cycloheteroalkyl or substituted cycloheteroalkyl.

23. The compound of any one of claims 1, 2, 4 or 5, wherein A is aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heteroaryl, substituted heteroaryl, heteroarylalkyl,

substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl or substituted cycloheteroalkenyl.

24. The compound of any one of claims 1, 2, 4 or 5, wherein A is aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl.

25. The compound of any one of claims 1, 2, 4 or 5, wherein A is aryl, substituted aryl, heteroaryl or substituted heteroaryl.

26. The compound of any one of claims 1, 3, 4 or 6, wherein B is aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylalkenyl, substituted arylalkenyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heteroarylalkenyl, substituted heteroarylalkenyl, cycloheteroalkyl, substituted cycloheteroalkyl, cycloheteroalkenyl or substituted cycloheteroalkenyl.

27. The compound of any one of claims 1, 3, 4 or 6, wherein B is aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl.

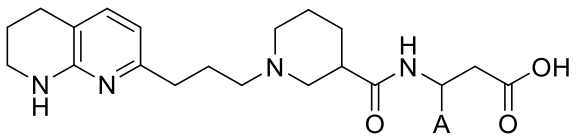
28. The compound of any one of claims 1, 3, 4 or 6, wherein B is aryl, substituted aryl, heteroaryl or substituted heteroaryl.

29. The compound of any one of claims 1, 3, 4 or 6, wherein B is $-NR_{53}R_{54}$.

30. The compound of any one of claims 1, 3, 4 or 6, wherein B is $-NHR_{54}$, R_{54} is aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl $-C(O)R_{58}$, $-C(O)OR_{59}$, or $-SO_2R_{62}$.

31. The compound of any one of claims 1, 3, 4 or 6, wherein B is $-NHR_{54}$ and R_{54} is aryl, substituted aryl, heteroaryl, substituted heteroaryl, $-C(O)R_{58}$, $-C(O)OR_{59}$, or $-SO_2R_{62}$.

32. The compound of claim 1 of Formula (VII):



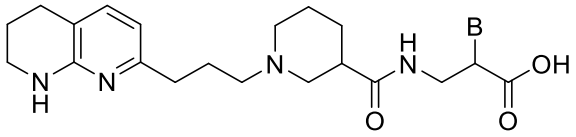
(VII)

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33. The compound of claim 32, wherein A is aryl, substituted aryl, heteroaryl or substituted heteroaryl.

34. The compound of claim 32, wherein A is aryl, substituted phenyl, heteroaryl or substituted heteroaryl.

35. The compound of claim 1 of Formula (VIII):



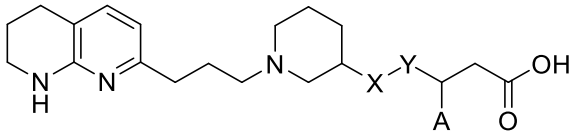
(VIII)

36. The compound of claim 35, wherein B is aryl, substituted aryl, heteroaryl or substituted heteroaryl.

37. The compound of claim 35, wherein B is aryl, substituted phenyl, heteroaryl or substituted heteroaryl.

38. The compound of claim 35, wherein B is -NHR_{54} and R_{54} is aryl, substituted aryl, heteroaryl, substituted heteroaryl, -$C(O)R_{58}$, -$C(O)OR_{59}$, or -SO_2R_{62}.

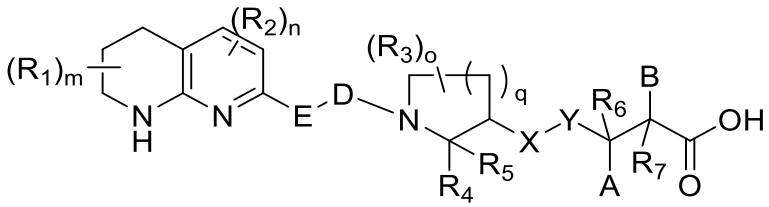
39. The compound of claim 1 of Formula (IX):



(IX)

40. The compound of claim 1, wherein A is phenyl or substituted phenyl.

41. A compound of Formula (Ia):



(Ia)

or pharmaceutically acceptable salts thereof, wherein:

q is 1, 2 or 3;

R^1 and R^3 are each independently selected at each occurrence from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-C(O)OR^{11}$, =O, =S, and $-CN$;

m is selected from 0, 1, 2, 3, 4, 5, and 6;

o is selected from 0, 1, 2, 3, 4, 5, 6, 7, and 8;

R^2 is independently selected at each occurrence from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{12}$, $-SR^{12}$, $-N(R^{12})_2$, $-CN$, and $-NO_2$;

n is 0, 1 or 2;

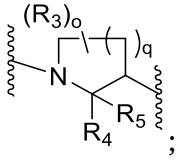
R^4 and R^5 are each independently selected from hydrogen, halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{13}$, $-SR^{13}$, $-N(R^{13})_2$, and $-CN$; or R^4 and R^5 are taken together to form a double bonded substituent selected from =O, =S and $=N(R^{13})$;

D is selected from a bond, $-C(O)-$, $-C\equiv CCH_2-$, and $-CH=CHCH_2-$;

E is selected from C_{1-4} alkylene and $-(CH_2)Z-$,

wherein Z is selected from $-NH-$, $-S-$, $-SO_2-$, and $-O-$;

X-Y is selected from: $^{\lambda}-C(O)N(R^{14})-$, $^{\lambda}-N(R^{14})C(O)-$, $^{\lambda}-N(R^{14})C(O)C(R^{15})_2-$, $^{\lambda}-C(O)O-$, $^{\lambda}-C(R^{15})_2C(R^{15})_2-$, $^{\lambda}-CH=CH-$, $^{\lambda}-C\equiv C-$, $^{\lambda}-N(R^{14})C(R^{15})_2-$, $^{\lambda}-C(R^{15})_2N(R^{14})-$, $^{\lambda}-O-$, $^{\lambda}-OC(R^{15})_2-$, $^{\lambda}-C(R^{15})_2O-$, $^{\lambda}-SO_2N(R^{14})-$, and $^{\lambda}-N(R^{14})SO_2-$;

wherein $^{\lambda}$ denotes the attachment of X-Y to 

;

R^6 and R^7 are each independently selected at each occurrence from:

hydrogen, halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, and $-CN$;

A is selected from (i) and (ii):

(i) hydrogen, halogen, and $-CN$, or A and R^6 come together to form a C_{3-6} carbocycle or 3- to 6-membered heterocycle;

(ii) $-OR^{17}$, $-SR^{17}$, $-N(R^{17})_2$, $-N(R^{17})C(O)R^{17}$, $-N(R^{17})C(O)OR^{17}$, $-N(R^{17})C(O)N(R^{17})_2$, $-N(R^{17})C(S)N(R^{17})_2$, $-N(R^{17})S(O)_2(R^{17})$, $-C(O)R^{17}$, $-C(O)OR^{17}$, $-OC(O)R^{17}$, $-OC(O)N(R^{17})_2$, $-C(O)N(R^{17})_2$, $-S(O)R^{17}$, $-S(O)_2R^{17}$, and $-S(O)_2N(R^{17})_2$;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{17}$, $-SR^{17}$, $-N(R^{17})_2$, $-C(O)R^{17}$, $-C(O)OR^{17}$, $-OC(O)R^{17}$, $-OC(O)N(R^{17})_2$, $-C(O)N(R^{17})_2$, $-N(R^{17})C(O)R^{17}$, $-N(R^{17})C(O)OR^{17}$, $-N(R^{17})C(O)N(R^{17})_2$, $-N(R^{17})C(S)N(R^{17})_2$, $-N(R^{17})S(O)_2(R^{17})$, $-S(O)R^{17}$, $-S(O)_2R^{17}$, $-S(O)_2N(R^{17})_2$, $-NO_2$, =O, =S, $=N(R^{17})$, $-N_3$, and $-CN$, C_{3-10} carbocycle, and 3- to 10-membered heterocycle,

wherein the C_{3-10} carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more substituents independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^{17}$, $-SR^{17}$, $-N(R^{17})_2$, $-C(O)R^{17}$, $-C(O)OR^{17}$, $-OC(O)R^{17}$, $-OC(O)N(R^{17})_2$, $-C(O)N(R^{17})_2$, $-N(R^{17})C(O)R^{17}$, $-N(R^{17})C(O)OR^{17}$, $-N(R^{17})C(O)N(R^{17})_2$, $-N(R^{17})C(S)N(R^{17})_2$, $-N(R^{17})S(O)_2(R^{17})$, $-S(O)R^{17}$, $-S(O)_2R^{17}$, $-S(O)_2N(R^{17})_2$, $-NO_2$, =O, =S, $=N(R^{17})$, $-N_3$, and $-CN$; and

C_{3-12} carbocycle and 3- to 12-membered heterocycle, any of which is optionally

substituted with one or more substituents independently selected from:

halogen, $-OR^{17}$, $-SR^{17}$, $-N(R^{17})_2$, $-C(O)R^{17}$, $-C(O)OR^{17}$, $-OC(O)R^{17}$, $-OC(O)N(R^{17})_2$, $-C(O)N(R^{17})_2$, $-N(R^{17})C(O)R^{17}$, $-N(R^{17})C(O)OR^{17}$, $-N(R^{17})C(O)N(R^{17})_2$, $-N(R^{17})C(S)N(R^{17})_2$, $-N(R^{17})S(O)_2(R^{17})$, $-S(O)R^{17}$, $-S(O)_2R^{17}$, $-S(O)_2N(R^{17})_2$, $-NO_2$, =O, =S, $=N(R^{17})$, $-N_3$, and −CN;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, $-OR^{17}$, $-SR^{17}$, $-N(R^{17})_2$, $-C(O)R^{17}$, $-C(O)OR^{17}$, $-OC(O)R^{17}$, $-OC(O)N(R^{17})_2$, $-C(O)N(R^{17})_2$, $-N(R^{17})C(O)R^{17}$, $-N(R^{17})C(O)OR^{17}$, $-N(R^{17})C(O)N(R^{17})_2$, $-N(R^{17})C(S)N(R^{17})_2$, $-N(R^{17})S(O)_2(R^{17})$, $-S(O)R^{17}$, $-S(O)_2R^{17}$, $-S(O)_2N(R^{17})_2$, $-NO_2$, =O, =S, $=N(R^{17})$, $-N_3$, and −CN; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, and =O;

B is selected from (I) when A is selected from (ii), or

B is selected from (II) when A is selected from (i):

(I) hydrogen, halogen, and -CN, or B and R^7 are taken together to form a C_{3-6} carbocycle or a 3- to 6-membered heterocycle;

(II) $-OR^{18}$, $-SR^{18}$, $-N(R^{18})_2$, $-C(O)R^{18}$, $-C(O)OR^{18}$, $-OC(O)R^{18}$, $-OC(O)N(R^{18})_2$, $-C(O)N(R^{18})_2$, $-N(R^{18})C(O)R^{18}$, $-N(R^{18})C(O)OR^{18}$, $-N(R^{18})C(O)N(R^{18})_2$, $-N(R^{18})C(S)N(R^{18})_2$, $-N(R^{18})S(O)_2(R^{18})$, $-S(O)R^{18}$, $-S(O)_2R^{18}$, and $-S(O)_2N(R^{18})_2$;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{18}$, $-SR^{18}$, $-N(R^{18})_2$, $-C(O)R^{18}$, $-C(O)OR^{18}$, $-OC(O)R^{18}$, $-OC(O)N(R^{18})_2$, $-C(O)N(R^{18})_2$, $-N(R^{18})C(O)R^{18}$, $-N(R^{18})C(O)OR^{18}$, $-N(R^{18})C(O)N(R^{18})_2$, $-N(R^{18})C(S)N(R^{18})_2$, $-N(R^{18})S(O)_2(R^{18})$, $-S(O)R^{18}$, $-S(O)_2R^{18}$, $-S(O)_2N(R^{18})_2$, $-NO_2$, =O, =S, $=N(R^{18})$, $-N_3$,−CN, C_{3-10} carbocycle and 3- to 10-membered heterocycle,

wherein the C_{3-10} carbocycle and 3- to 10-membered heterocycle are optionally substituted with one or more substituents independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^{18}$, $-SR^{18}$, $-N(R^{18})_2$, $-C(O)R^{18}$, $-C(O)OR^{18}$, $-OC(O)R^{18}$, $-OC(O)N(R^{18})_2$, $-C(O)N(R^{18})_2$, $-N(R^{18})C(O)R^{18}$, $-N(R^{18})C(O)OR^{18}$, $-N(R^{18})C(O)N(R^{18})_2$,

$-N(R^{18})C(S)N(R^{18})_2$, $-N(R^{18})S(O)_2(R^{18})$, $-S(O)R^{18}$, $-S(O)_2R^{18}$, $-S(O)_2N(R^{18})_2$, $-NO_2$, =O, =S, $=N(R^{18})$, $-N_3$, and −CN; and

C_{3-12} carbocycle and 3- to 12-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{18}$, $-SR^{18}$, $-N(R^{18})_2$, $-C(O)R^{18}$, $-C(O)OR^{18}$, $-OC(O)R^{18}$, $-OC(O)N(R^{18})_2$, $-C(O)N(R^{18})_2$, $-N(R^{18})C(O)R^{18}$, $-N(R^{18})C(O)OR^{18}$, $-N(R^{18})C(O)N(R^{18})_2$, $-N(R^{18})C(S)N(R^{18})_2$, $-N(R^{18})S(O)_2(R^{18})$, $-S(O)R^{18}$, $-S(O)_2R^{18}$, $-S(O)_2N(R^{18})_2$, $-NO_2$, =O, =S, $=N(R^{18})$, $-N_3$, and −CN;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{18}$, $-SR^{18}$, $-N(R^{18})_2$, $-C(O)R^{18}$, $-C(O)OR^{18}$, $-OC(O)R^{18}$, $-OC(O)N(R^{18})_2$, $-C(O)N(R^{18})_2$, $-N(R^{18})C(O)R^{18}$, $-N(R^{18})C(O)OR^{18}$, $-N(R^{18})C(O)N(R^{18})_2$, $-N(R^{18})C(S)N(R^{18})_2$, $-N(R^{18})S(O)_2(R^{18})$, $-S(O)R^{18}$, $-S(O)_2R^{18}$, $-S(O)_2N(R^{18})_2$, $-NO_2$, =O, =S, $=N(R^{18})$, $-N_3$,–CN, C_{3-6} carbocycle and 3- to 6-membered heterocycle,

wherein the C_{3-6} carbocycle and 3- to 6-membered heterocycle are each optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, and =O; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, and =O;

R^{11}, R^{12}, R^{13}, R^{14}, and R^{16} are each independently selected at each occurrence from hydrogen, C_{1-4} alkyl, and C_{1-4} haloalkyl;

R^{15} is independently selected at each occurrence from hydrogen, halogen, C_{1-4} alkyl, and C_{1-4} haloalkyl;

R^{17} is independently selected at each occurrence from:

hydrogen;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{21}$, $-SR^{21}$, $-N(R^{21})_2$, $-C(O)R^{21}$, $-C(O)OR^{21}$, $-OC(O)R^{21}$, $-OC(O)N(R^{21})_2$, $-C(O)N(R^{21})_2$, $-N(R^{21})C(O)R^{21}$, $-NO_2$, =O, =S, $=N(R^{21})$, $-N_3$, and −CN; and

C_{3-6} carbocycle and 3- to 6-membered heterocycle, any of which are optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{21}$, $-SR^{21}$, $-N(R^{21})_2$, $-C(O)R^{21}$, $-C(O)OR^{21}$, $-OC(O)R^{21}$, $-OC(O)N(R^{21})_2$, $-C(O)N(R^{21})_2$,

$-N(R^{21})C(O)R^{21}$, $-N(R^{21})C(O)OR^{21}$, $-N(R^{21})C(O)N(R^{21})_2$, $-N(R^{21})C(S)N(R^{21})_2$, $-N(R^{21})S(O)_2(R^{21})$, $-S(O)R^{21}$, $-S(O)_2R^{21}$, $-S(O)_2N(R^{21})_2$, $-NO_2$, =O, =S, $=N(R^{21})$, $-N_3$, and −CN;

R^{18} is independently selected at each occurrence from:

hydrogen;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{22}$, $-SR^{22}$, $-N(R^{22})_2$, $-C(O)R^{22}$, $-C(O)OR^{22}$, $-OC(O)R^{22}$, $-OC(O)N(R^{22})_2$, $-C(O)N(R^{22})_2$, $-N(R^{22})C(O)R^{22}$, $-NO_2$, =O, =S, $=N(R^{22})$, $-N_3$, −CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle,

wherein the C_{3-10} carbocycle and 3- to 10-membered heterocycle each are optionally substituted with one or more substituents independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^{22}$, $-SR^{22}$, and $-N(R^{22})_2$; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^{22}$, $-SR^{22}$, $-N(R^{22})_2$, $-C(O)R^{22}$, $-C(O)OR^{22}$, $-OC(O)R^{22}$, $-OC(O)N(R^{22})_2$, $-C(O)N(R^{22})_2$, $-N(R^{22})C(O)R^{22}$, $-N(R^{22})C(O)OR^{22}$, $-N(R^{22})C(O)N(R^{22})_2$, $-N(R^{22})C(S)N(R^{22})_2$, $-N(R^{22})S(O)_2(R^{22})$, $-S(O)R^{22}$, $-S(O)_2R^{22}$, $-S(O)_2N(R^{22})_2$, $-NO_2$, =O, =S, $=N(R^{22})$, $-N_3$,−CN, C_{3-6} carbocycle, and 3- to 6-membered heterocycle;

wherein the C_{3-6} carbocycle and 3- to 6-membered heterocycle are each optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, and C_{1-4} haloalkyl;

R^{21} and R^{22} are each independently selected at each occurrence from:

hydrogen;

C_{1-4} alkyl optionally substituted with one or more substituents independently selected from halogen, hydroxyl, C_{3-6} carbocycle, and 3- to 6-membered heterocycle, wherein each C_{3-6} carbocycle and 3- to 6-membered heterocycle is optionally substituted with one or more substituents independently selected from C_{1-4} alkyl, $-N(R^{23})_2$, and $-C(O)N(R^{23})_2$; and

C_{3-6} carbocycle and 3- to 12-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, and =O; and

R^{23} is independently selected at each occurrence from hydrogen and C_{1-4} alkyl.

42. The compound or salt of claim 41, wherein R^3 is selected at each occurrence from halogen, C_{1-4} alkyl, and $-C(O)N(R^{11})_2$; and o is 0, 1, or 2.
43. The compound or salt of claim 41 or 42, wherein q is 1 or 2.
44. The compound or salt of any one of claims 41 to 43, wherein m is 0 and n is 0.
45. The compound or salt of any one of claims 41 to 44, wherein R^4 and R^5 are each hydrogen.
46. The compound or salt of any one of claims 41 to 45, wherein D is a bond or $-C(O)-$.
47. The compound or salt of any one of claims 41 to 46, wherein E is selected from C_{1-4} alkylene.
48. The compound or salt of any one of claims 41 to 47, wherein X-Y is selected from $^{\lambda}-C(O)N(R^{14})-$, $^{\lambda}-N(R^{14})C(O)-$, $^{\lambda}-N(R^{14})C(O)CH_2-$, $^{\lambda}-CH_2CH_2-$, $^{\lambda}-N(R^{14})CH_2-$, $^{\lambda}-CH_2N(R^{14})-$, $^{\lambda}-O-$, $^{\lambda}-OCH_2-$, and $^{\lambda}-CH_2O-$; and R^{14} is selected at each occurrence from hydrogen and C_{1-4} alkyl.
49. The compound or salt of claim 48, wherein X-Y is selected from $^{\lambda}-C(O)N(R^{14})-$, $^{\lambda}-N(R^{14})C(O)-$, and $^{\lambda}-OCH_2-$; and R^{14} is hydrogen.
50. The compound or salt of any one of claims 41 to 49, wherein R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, and R^{16} are each selected at each occurrence from hydrogen.
51. The compound or salt of any one of claims 41 to 50, wherein R^6 is selected from hydrogen and $-OH$, or A and R^6 are taken together to form a C_{3-6} carbocycle; and R^7 is selected from hydrogen and halogen.
52. The compound or salt of any one of claims 41 to 51, wherein R^6 and R^7 are each selected from hydrogen.
53. The compound or salt of any one of claims 41 to 52, wherein A is selected from hydrogen, halogen, and $-CN$, or A and R^6 are taken together to form a C_{3-6} carbocycle.
54. The compound or salt of claim 53, wherein A is hydrogen.
55. The compound or salt of any one of claims 41 to 52, wherein B is selected from hydrogen, halogen, and $-CN$.
56. The compound or salt of claim 55, wherein B is selected from hydrogen and halogen.
57. The compound or salt of any one of claims 41 to 50 and 55 to 56, wherein A is selected from C_{3-12} carbocycle and 3- to 12-membered heterocycle, any of which is optionally substituted with one or more substituents.
58. The compound or salt of claim 57, wherein the C_{3-12} carbocycle and 3- to 12-membered heterocycle of A are selected from phenyl; pyridine; indane; chromane; benzodioxole; 2,3-dihydrobenzofuran; quinoline; 1,2,3,4-tetrahydronaphthalene; naphthalene; quinoxaline; 2',3'-dihydrospiro[cyclopropane-1,1'-indene]; and pyrazole; any of which is optionally substituted with one or more substituents.

59. The compound or salt of claim 57 or claim 58, wherein the one or more optional substituents on A are selected from:

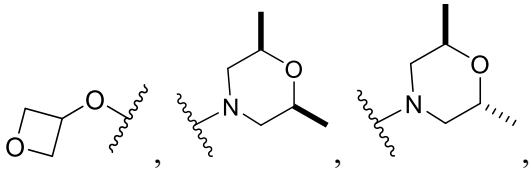
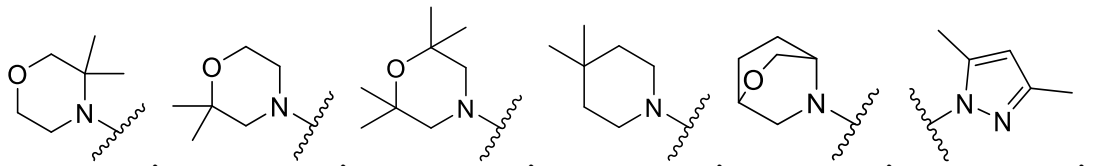
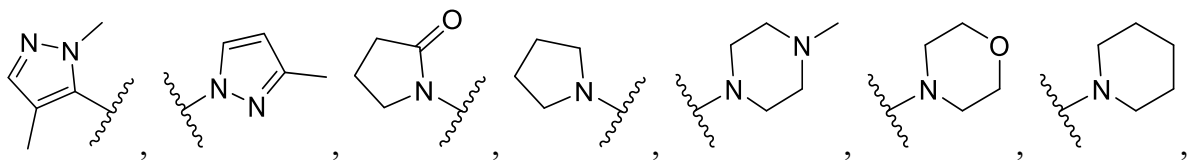
halogen, $-OR^{17}$, $N(R^{17})_2$, $-C(O)R^{17}$, $-N(R^{17})C(O)R^{17}$, $-N(R^{17})S(O)_2(R^{17})$, =O, =S, and $-CN$;

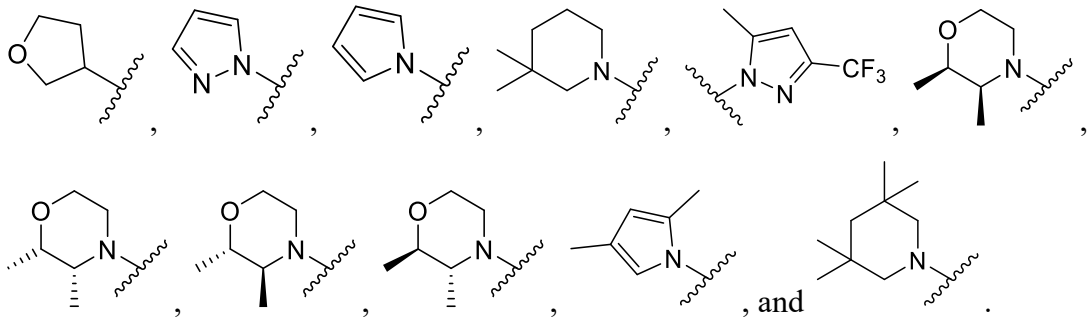
C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, $-OR^{17}$, $-N(R^{17})_2$, $-N(R^{17})C(O)R^{17}$, $-N(R^{17})S(O)_2(R^{17})$, $-S(O)R^{17}$, =O, and $-CN$; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, and =O.

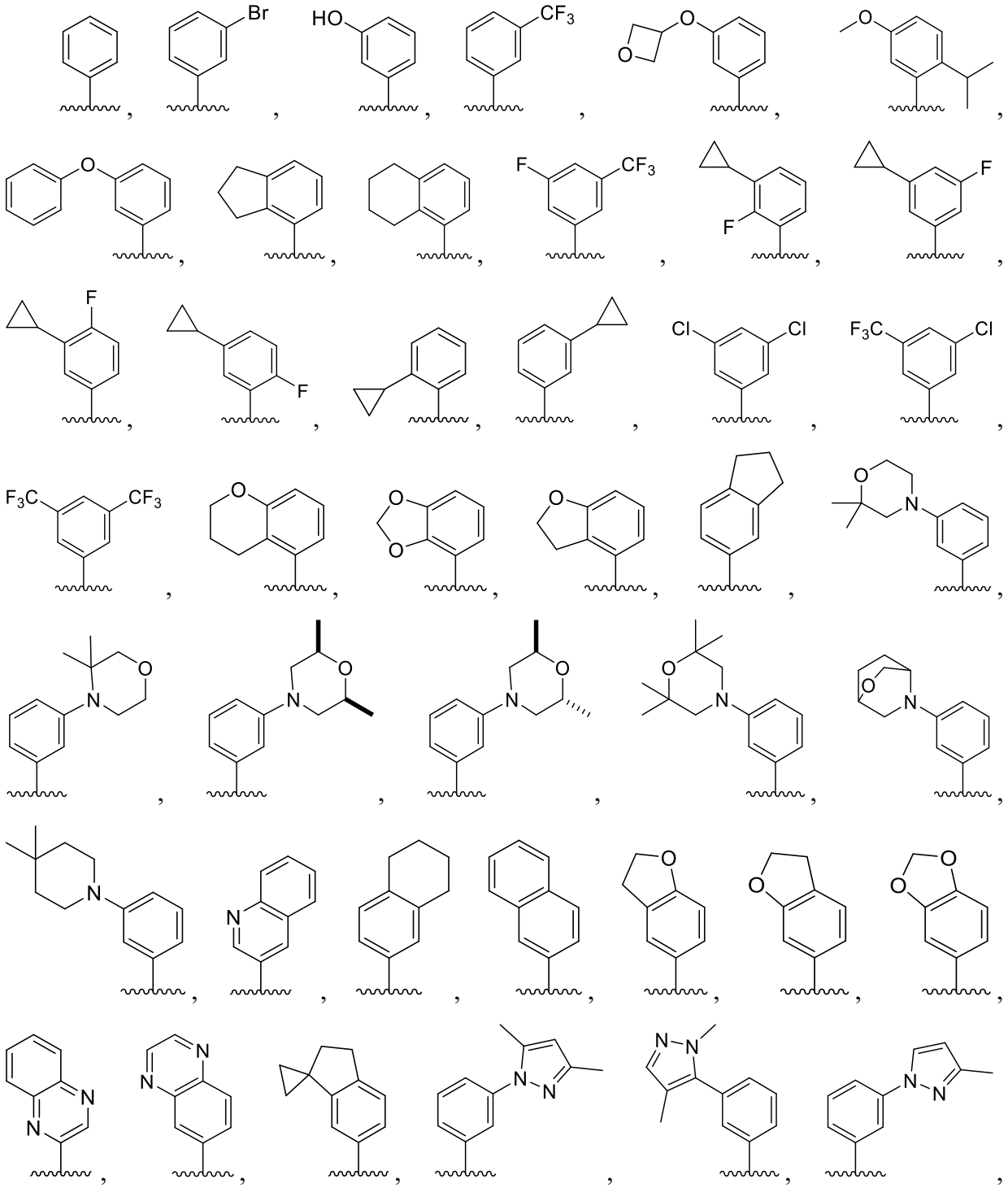
60. The compound or salt of claim 59, wherein the one or more optional substituents on A are selected from: halogen, $-OR^{17}$, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein the C_{3-10} carbocycle, and 3- to 10-membered heterocycle are each optionally substituted with one or more substituents independently selected from C_{1-4} alkyl, C_{1-4} haloalkyl, and =O.

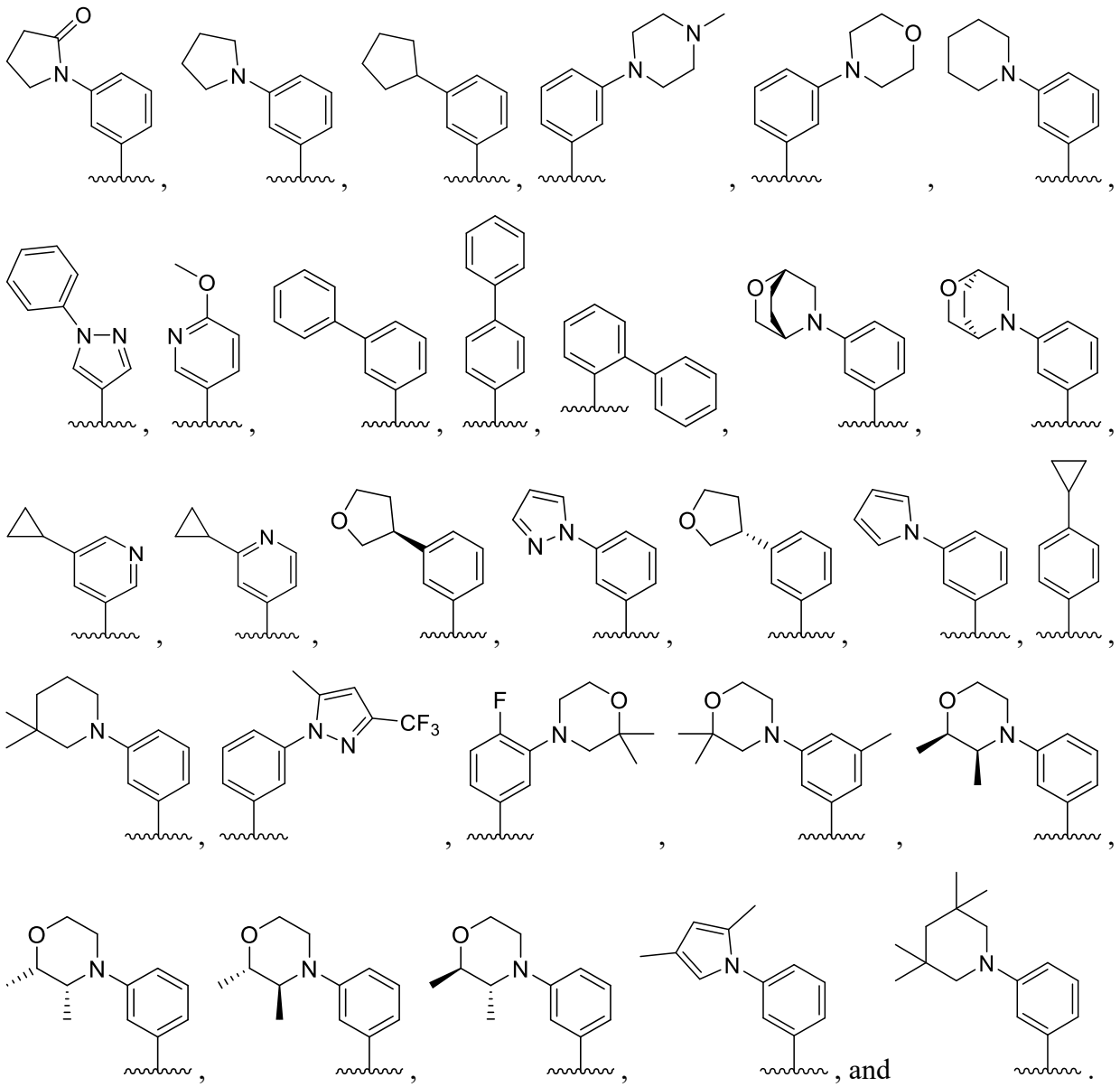
61. The compound or salt of any one of claims 41 to 52 and 55 to 60, wherein R^{17} is independently selected at each occurrence from hydrogen, C_{1-6} alkyl, C_{3-6} carbocycle and 3- to 6-membered heterocycle.

62. The compound or salt of any one of claims 41 to 52 and 57 to 61, wherein the one or more optional substituents on A is selected from: halogen, hydroxyl, methoxy, trifluoromethyl, propyl, cyclopropyl, cyclopentyl, phenyl, phenoxy, , , ,



63. The compound or salt of any one of claims 41 to 52 and 55 to 56, wherein A is selected from:





64. The compound or salt of any one of claims 41 to 54, wherein B is selected from:

$-OR^{18}$, $-SR^{18}$, $-N(R^{18})_2$, $-C(O)R^{18}$, $-C(O)OR^{18}$, $-OC(O)R^{18}$, $-OC(O)N(R^{18})_2$, $-C(O)N(R^{18})_2$, $-N(R^{18})C(O)R^{18}$, $-N(R^{18})C(O)OR^{18}$, $-N(R^{18})C(O)N(R^{18})_2$, $-N(R^{18})C(S)N(R^{18})_2$, $-N(R^{18})S(O)_2(R^{18})$, $-S(O)R^{18}$, $-S(O)_2R^{18}$, and $-S(O)_2N(R^{18})_2$;

C_{3-12} carbocycle, and 3- to 12-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{18}$, $-SR^{18}$, $-N(R^{18})_2$, $-C(O)R^{18}$, $-C(O)OR^{18}$, $-OC(O)R^{18}$, $-OC(O)N(R^{18})_2$, $-C(O)N(R^{18})_2$, $-N(R^{18})C(O)R^{18}$, $-N(R^{18})C(O)OR^{18}$, $-N(R^{18})C(O)N(R^{18})_2$, $-N(R^{18})C(S)N(R^{18})_2$, $-N(R^{18})S(O)_2(R^{18})$, $-S(O)R^{18}$, $-S(O)_2R^{18}$, $-S(O)_2N(R^{18})_2$, $-NO_2$, =O, =S, $=N(R^{18})$, $-N_3$, and $-CN$;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{18}$, $-SR^{18}$, $-N(R^{18})_2$, $-C(O)R^{18}$, $-C(O)OR^{18}$, $-OC(O)R^{18}$, $-OC(O)N(R^{18})_2$, $-C(O)N(R^{18})_2$, $-N(R^{18})C(O)R^{18}$, $-N(R^{18})C(O)OR^{18}$, $-N(R^{18})C(O)N(R^{18})_2$, $-N(R^{18})C(S)N(R^{18})_2$, $-N(R^{18})S(O)_2(R^{18})$, $-S(O)R^{18}$, $-S(O)_2R^{18}$, $-S(O)_2N(R^{18})_2$, $-NO_2$, =O, =S, $-N_3$,–CN, C_{3-6} carbocycle, and 3- to 6-membered heterocycle,

wherein the C_{3-6} carbocycle and 3- to 6-membered heterocycle are each optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, and =O; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, and =O.

65. The compound or salt of claim 64, wherein B is selected from $-OR^{18}$, $-SR^{18}$, $-N(R^{18})_2$, $-C(O)R^{18}$, $-C(O)OR^{18}$, $-OC(O)R^{18}$, $-OC(O)N(R^{18})_2$, $-C(O)N(R^{18})_2$, $-N(R^{18})C(O)R^{18}$, $-N(R^{18})C(O)OR^{18}$, $-N(R^{18})C(O)N(R^{18})_2$, $-N(R^{18})C(S)N(R^{18})_2$, $-N(R^{18})S(O)_2(R^{18})$, $-S(O)R^{18}$, $-S(O)_2R^{18}$, and $-S(O)_2N(R^{18})_2$.

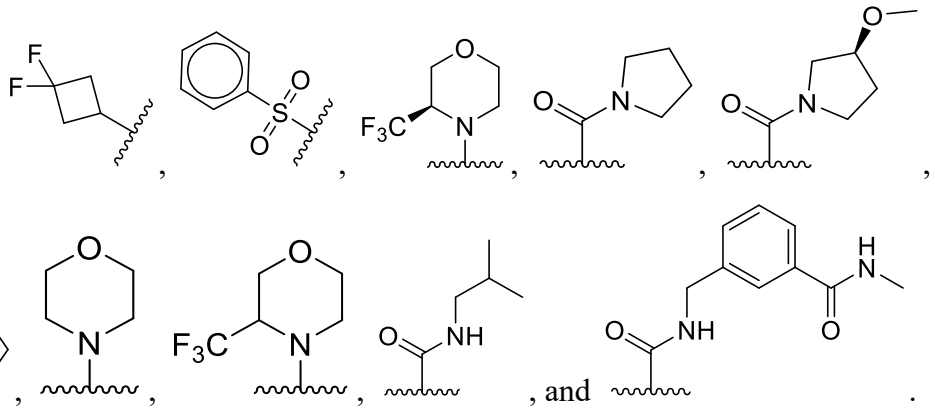
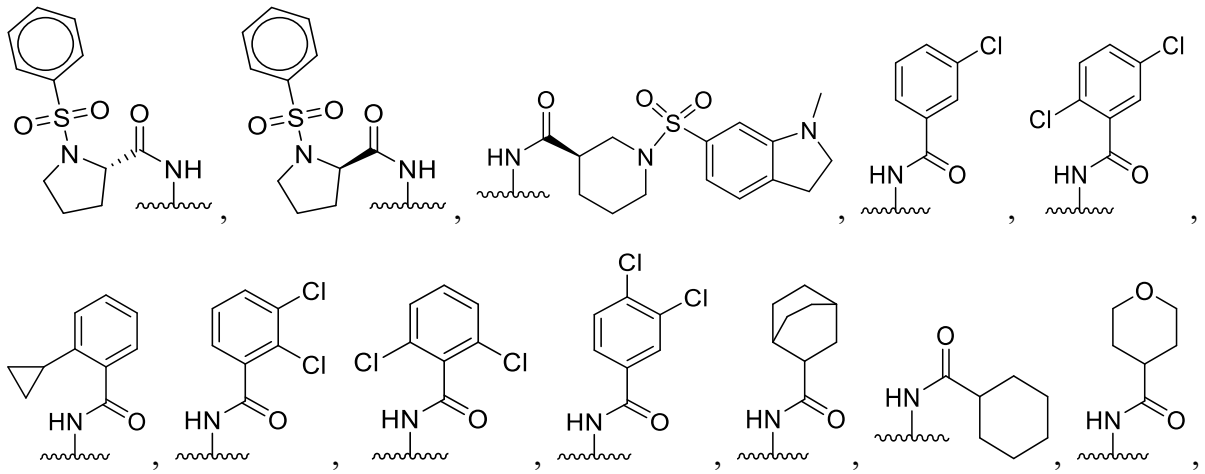
66. The compound or salt of claim 65, wherein B is selected from $-N(R^{18})_2$, $-N(R^{18})C(O)R^{18}$, $-N(R^{18})C(O)OR^{18}$, $-N(R^{18})C(O)N(R^{18})_2$, and $-N(R^{18})S(O)_2(R^{18})$.

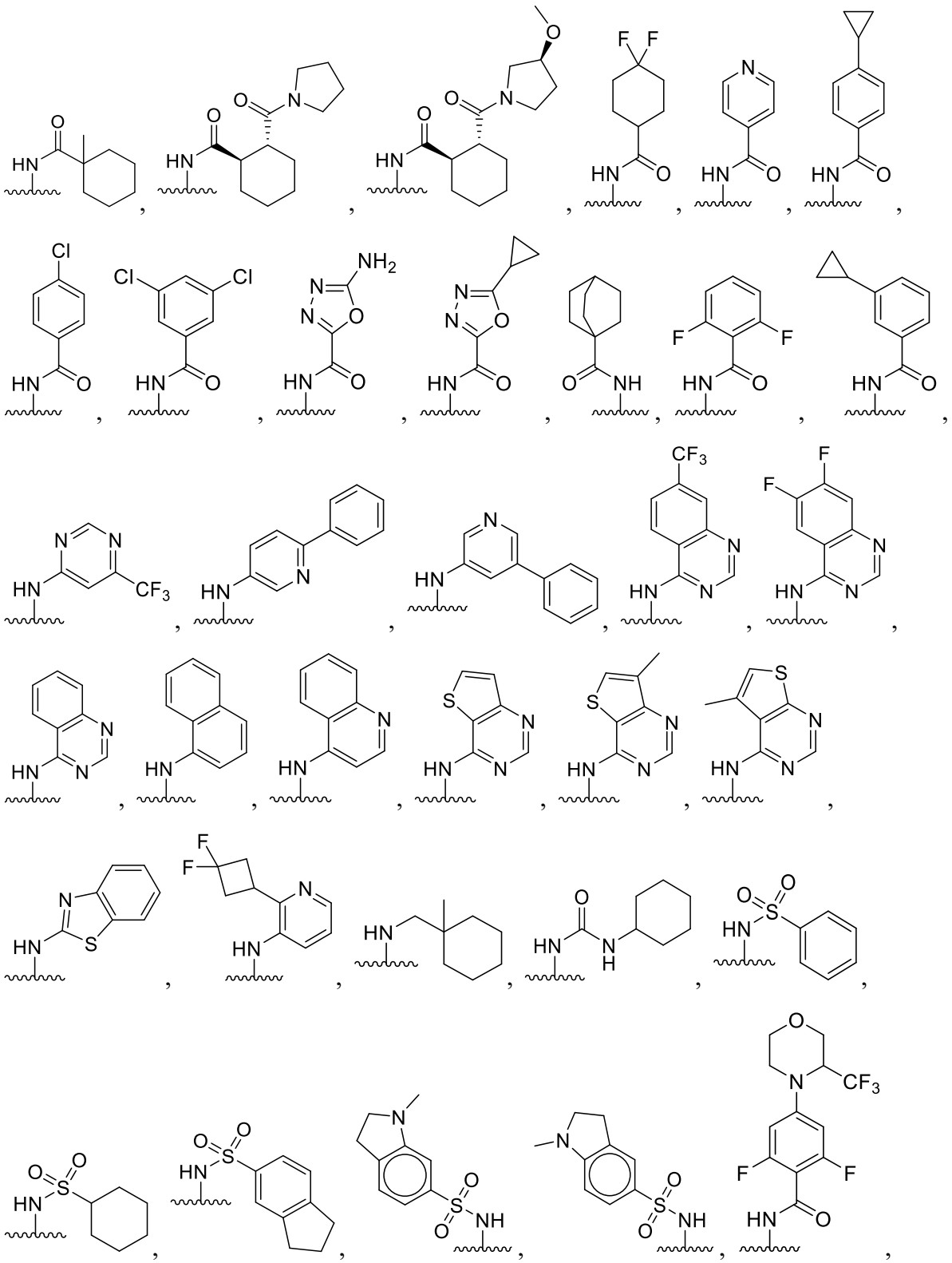
67. The compound or salt of any one of claims 64 to 66, wherein R^{18} is independently selected at each occurrence from hydrogen, C_{1-6} alkyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein the C_{1-6} alkyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle are each optionally substituted with one or more substituents.

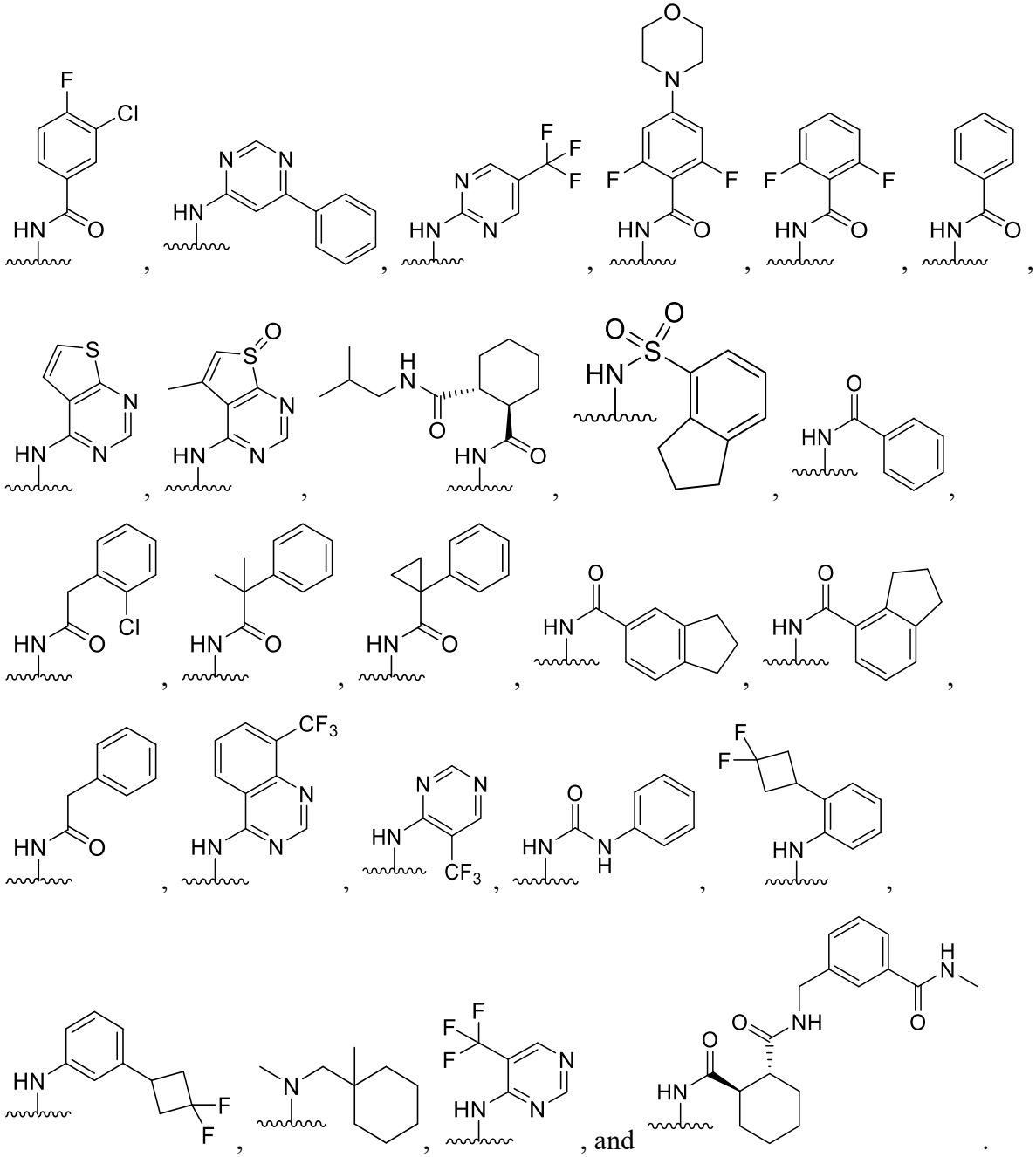
68. The compound or salt of any one of claims 64 to 67, wherein the C_{3-10} carbocycle and 3- to 10-membered heterocycle of R^{18} is independently selected at each occurrence from pyrrolidine, piperidine, phenyl, indoline, bicyclo[2.2.2]octane, cyclohexane, tetrahydropyran, pyridine, oxadiazole, pyrimidine, quinazoline, naphthalene, quinoline, thieno[3,2-*d*]pyrimidine, thieno[2,3-*d*]pyrimidine, benzothiazole, indane, thieno[2,3-*d*]pyrimidine oxide, and cyclopropyl, any of which is optionally substituted with one or more substituents.

69. The compound or salt of any one of claims 64 to 68, wherein the C_{3-10} carbocycle and 3- to 10-membered heterocycle of R^{18} are each optionally substituted at each occurrence with one or more substituents independently selected from: halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^{22}$, $-N(R^{22})_2$, $-C(O)R^{22}$, $-C(O)N(R^{22})_2$, $-N(R^{22})C(O)R^{22}$, $-S(O)_2R^{22}$, =O, -CN, C_{3-6} carbocycle, and 3- to 6-membered heterocycle, wherein the C_{3-6} carbocycle and 3- to 6-membered heterocycle

are each optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, and C_{1-4} haloalkyl.

70. The compound or salt of claim 69, wherein the C_{3-10} carbocycle and 3- to 10-membered heterocycle of R^{18} are each optionally substituted at each occurrence with one or more substituents independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, $-N(R^{22})_2$, $-C(O)R^{22}$, $-C(O)N(R^{22})_2$, $-S(O)_2R^{22}$, =O, C_{3-6} carbocycle, and 3- to 6-membered heterocycle, wherein the C_{3-6} carbocycle and 3- to 6-membered heterocycle are each optionally substituted with one or more substituents independently selected from halogen and C_{1-4} haloalkyl.
71. The compound or salt of any one of claims 64 to 70, wherein R^{22} is independently selected at each occurrence from hydrogen, C_{1-4} alkyl, C_{3-6} carbocycle, and 3- to 6-membered heterocycle, wherein the C_{3-6} carbocycle and 3- to 6-membered heterocycle are each optionally substituted with one or more substituents independently selected from C_{1-4} alkyl and C_{1-4} alkoxy.
72. The compound or salt of any one of claims 64 to 71, wherein the C_{3-10} carbocycle and 3- to 10-membered heterocycle of R^{18} are each optionally substituted at each occurrence with one or more substituents independently selected from: halogen, methyl, trifluoromethyl, cyclopropyl, phenyl, $-NH_2$, =O, , and .
73. The compound or salt of any one of claims 41 to 54, wherein B is selected from: 





74. The compound or salt of claim 64, wherein B is selected from C_{3-12} carbocycle and 3- to 12-membered heterocycle, any of which is optionally substituted with one or more substituents.

75. The compound or salt of claim 74, wherein the C_{3-12} carbocycle and 3- to 12-membered heterocycle of B is selected from phenyl; pyridinyl, naphthyl; 1,2,3,4-tetrahydronaphthalene; indane; 7-azaindole; indazole; and chromane; any of which is optionally substituted with one or more substituents.

76. The compound or salt of any of claims 74 to 75, wherein the C_{3-12} carbocycle and 3- to 12-membered heterocycle of B are each optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{18}$, $-N(R^{18})_2$, $-C(O)R^{18}$, =O, and $-CN$;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, $-OR^{18}$, $-SR^{18}$, $-N(R^{18})_2$, $-C(O)R^{18}$, =O, $-CN$, C_{3-6} carbocycle, and 3- to 6-membered heterocycle, wherein the C_{3-6} carbocycle and 3- to 6-membered heterocycle are each optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, and =O; and

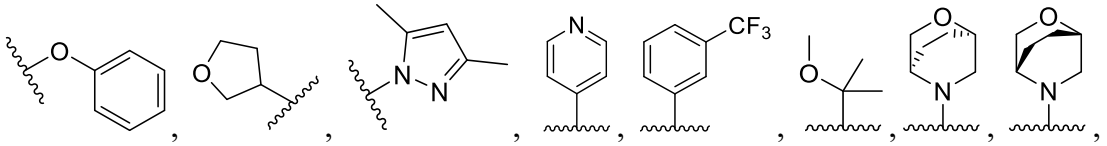
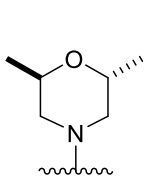
C_{3-10} carbocycle and 3- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, and =O.

77. The compound or salt of claims 76, wherein the C_{3-12} carbocycle and 3- to 12-membered heterocycle of B are each optionally substituted with one or more substituents independently selected from:

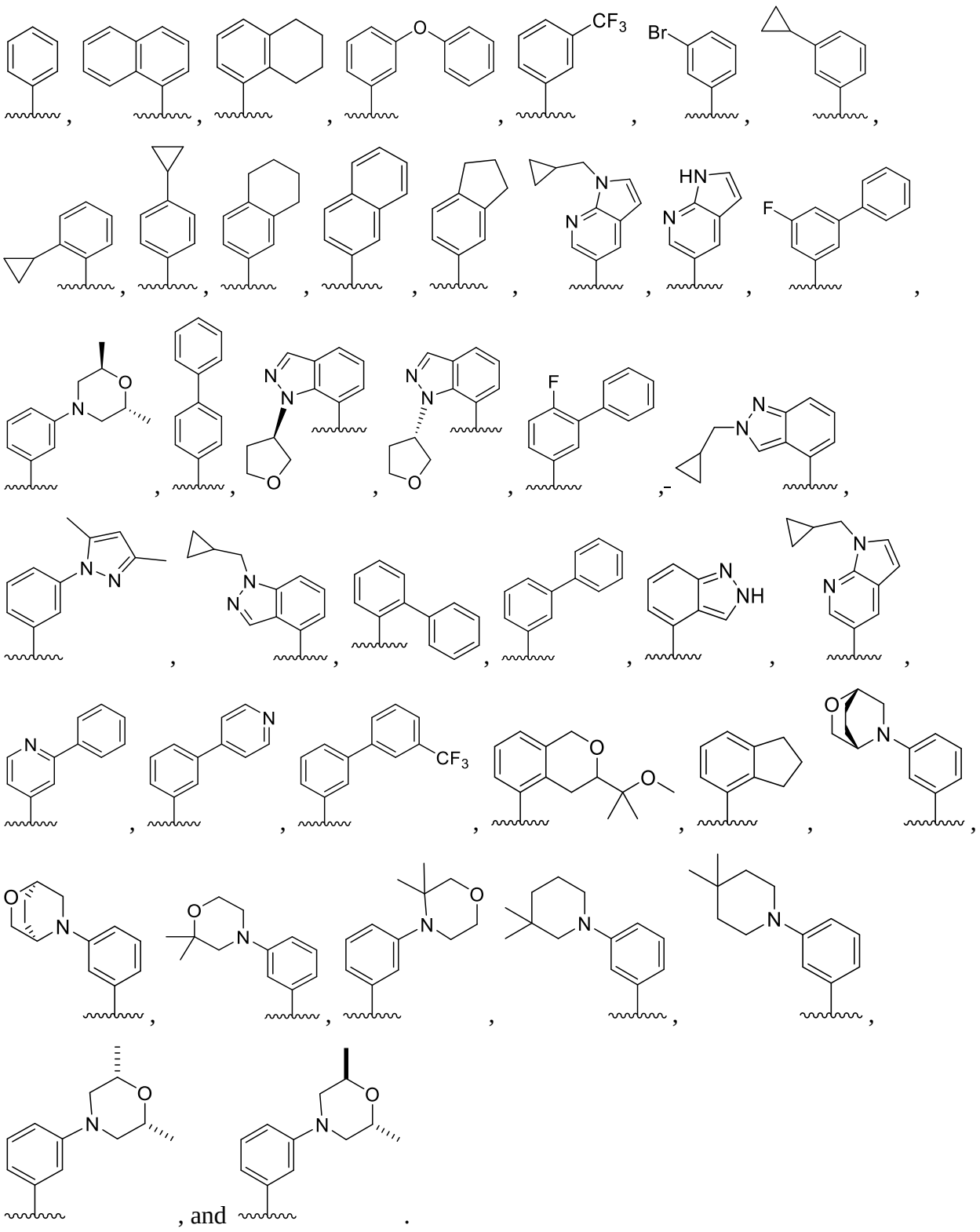
halogen and $-OR^{18}$;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, OR^{18}, and C_{3-6} carbocycle; and

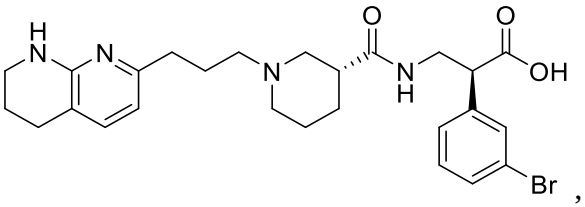
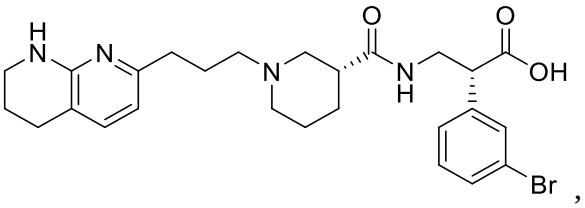
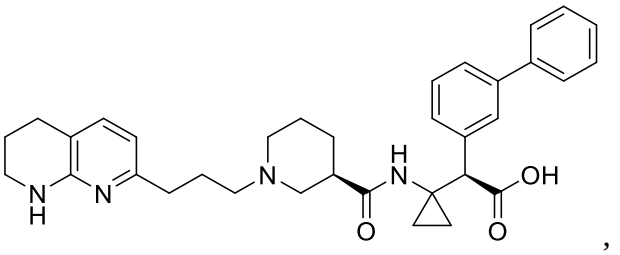
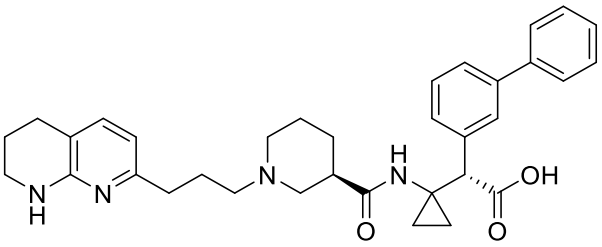
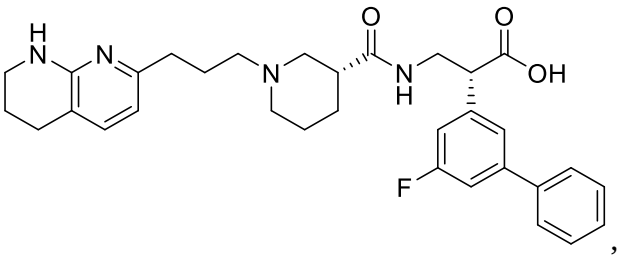
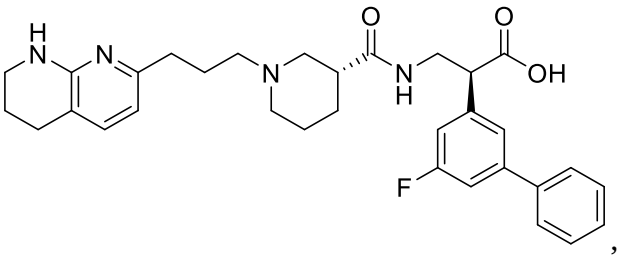
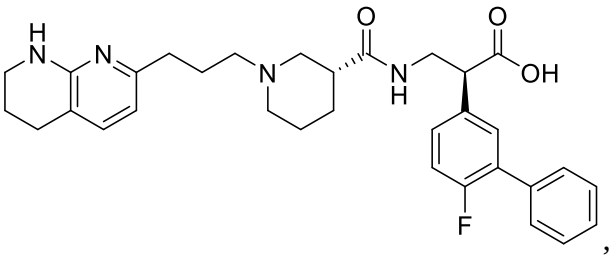
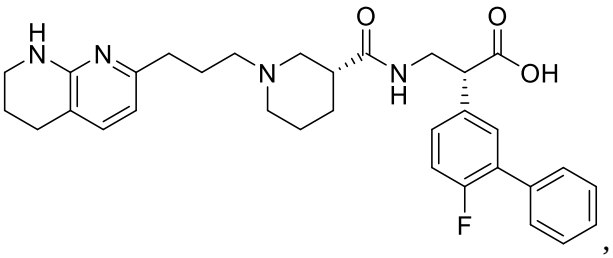
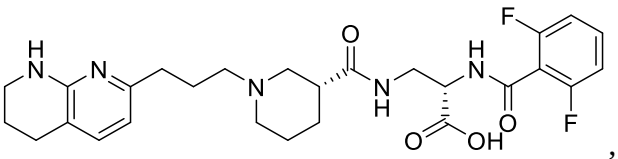
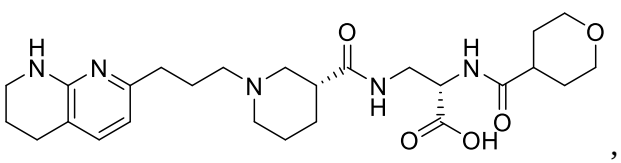
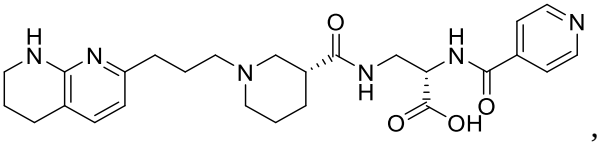
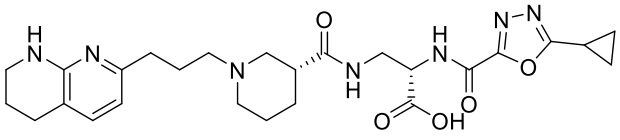
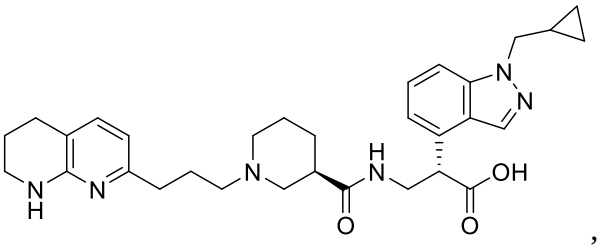
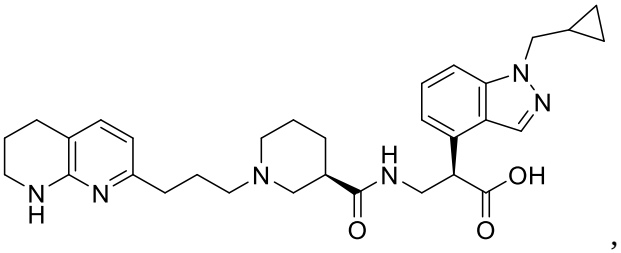
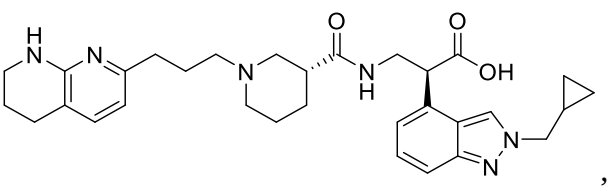
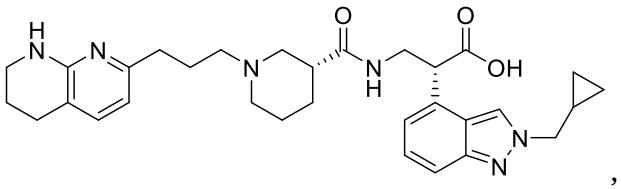
C_{3-10} carbocycle and 3- to 10-membered heterocycle, wherein the C_{3-10} carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more substituents independently selected from halogen and C_{1-4} alkyl.

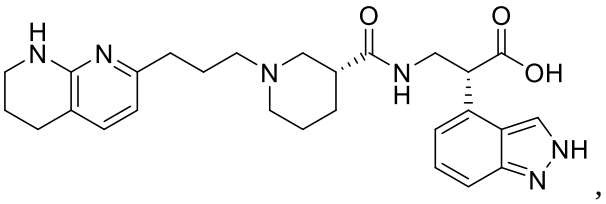
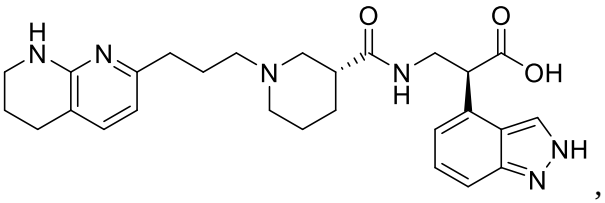
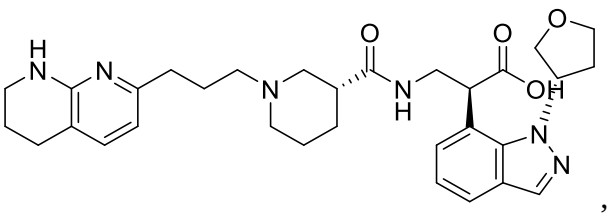
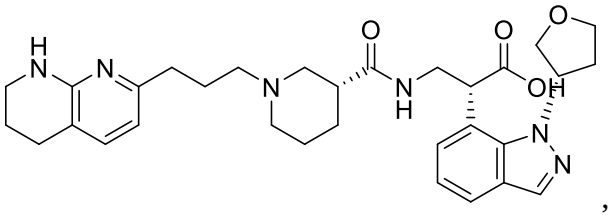
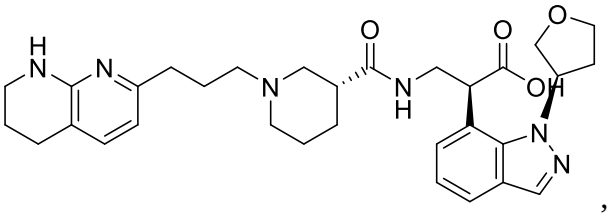
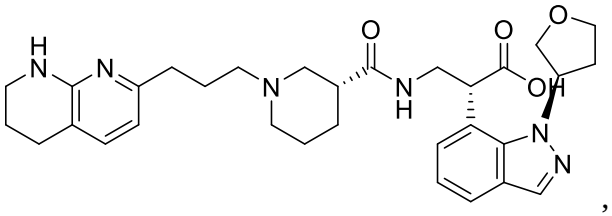
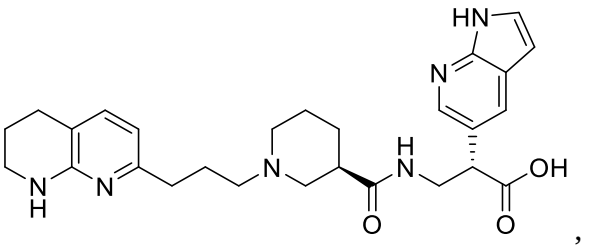
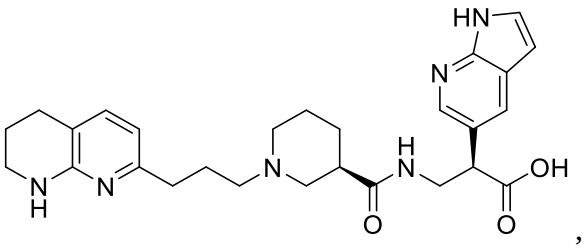
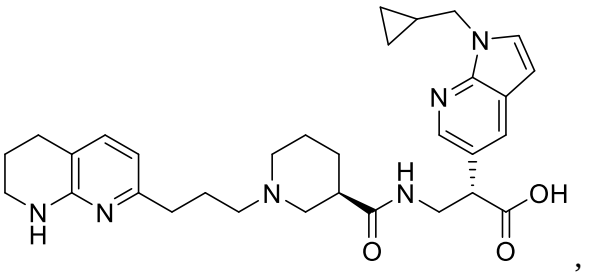
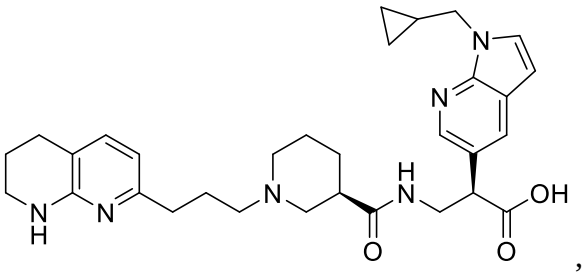
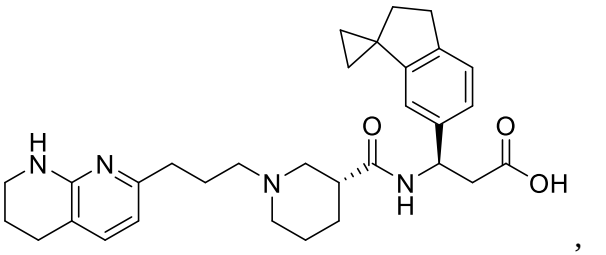
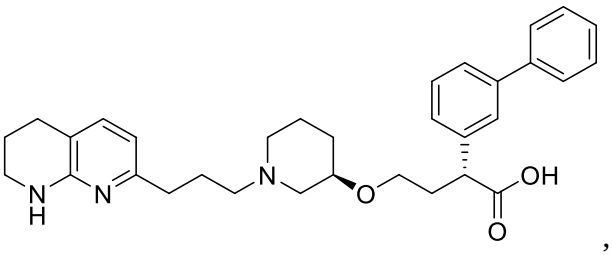
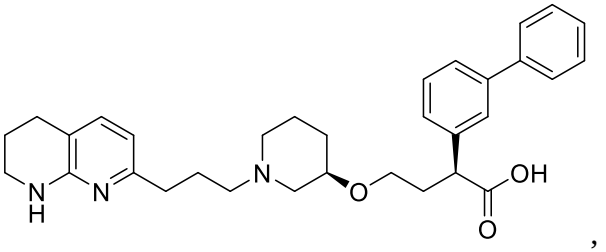
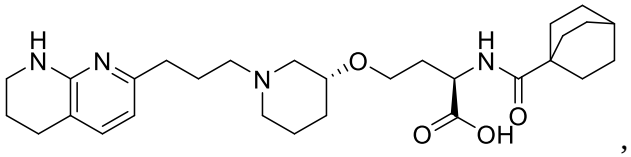
78. The compound or salt of any of claims 74 to 77, wherein the C_{3-12} carbocycle and 3- to 12-membered heterocycle of B are each optionally substituted with one or more substituents independently selected from halogen, trifluoromethyl, cyclopropyl, phenyl, , , and .

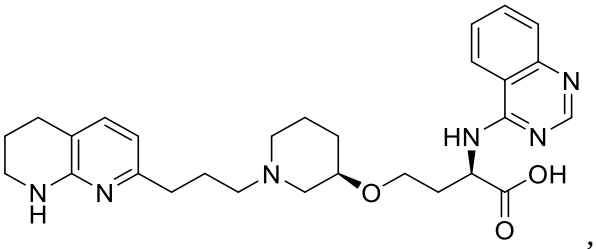
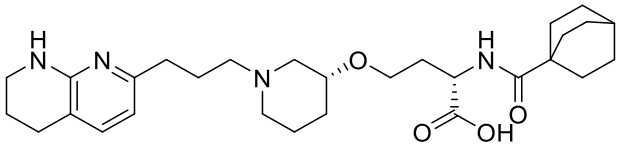
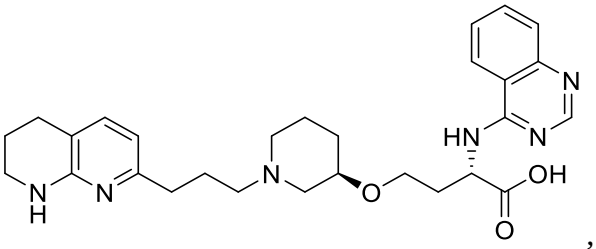
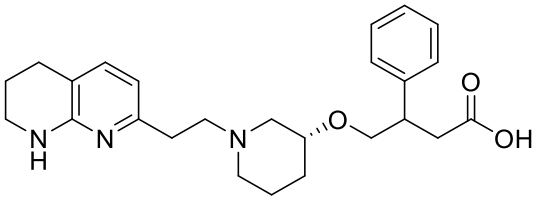
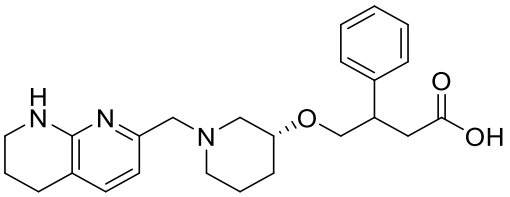
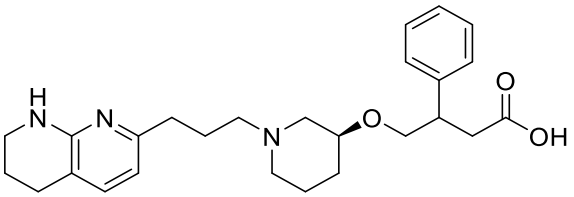
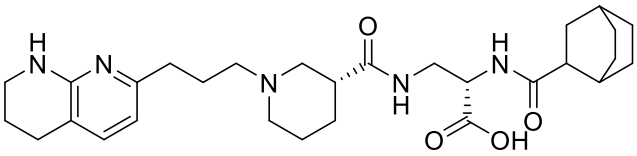
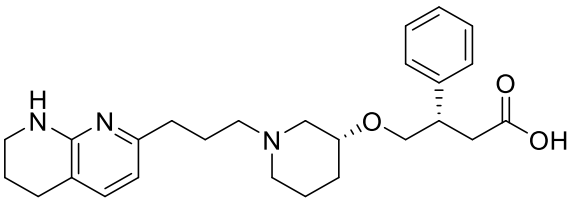
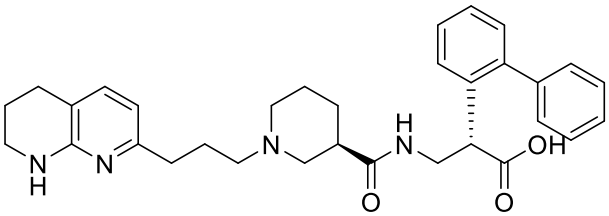
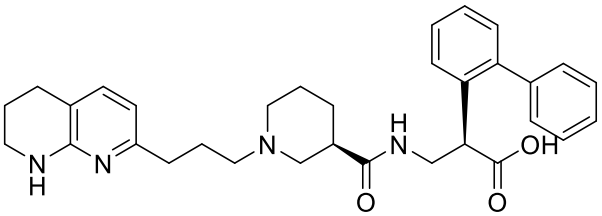
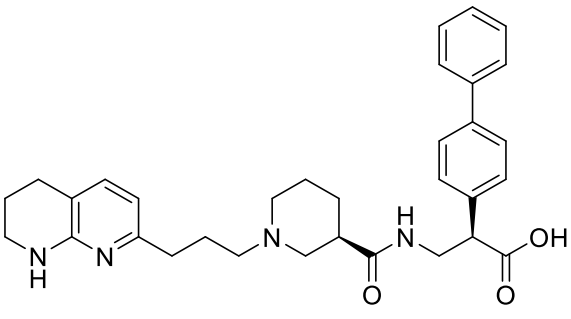
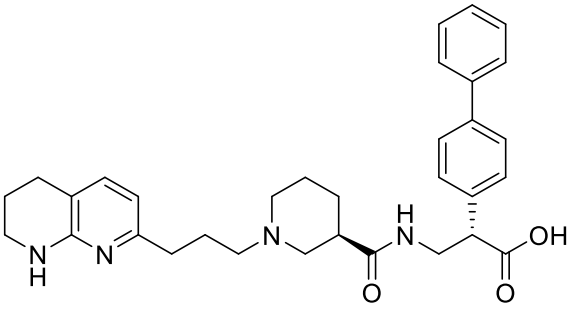
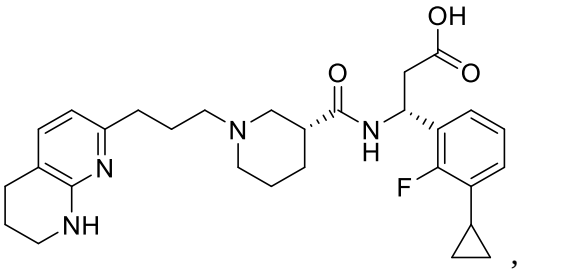
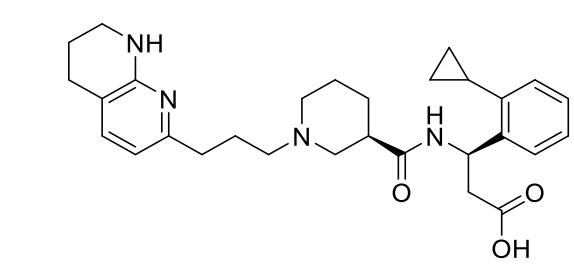
79. The compound or salt of any of claims 51 to 54, wherein B is selected from:



80. The compound or salt of claim 41, wherein the compound of Formula (Ia) is selected from:

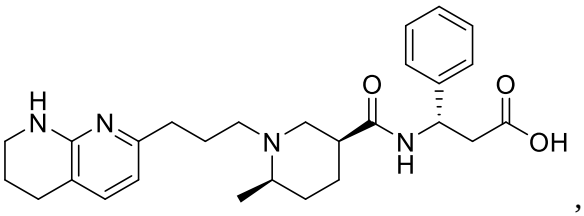
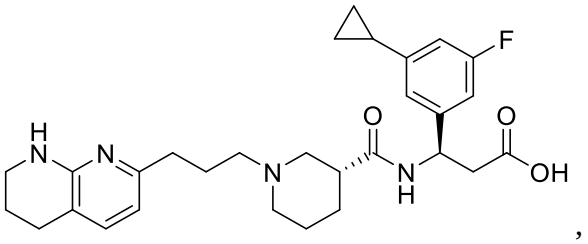
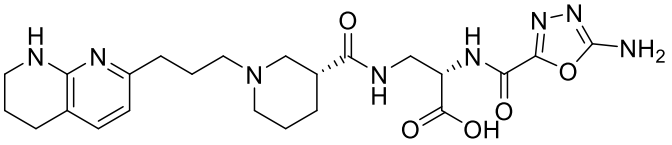
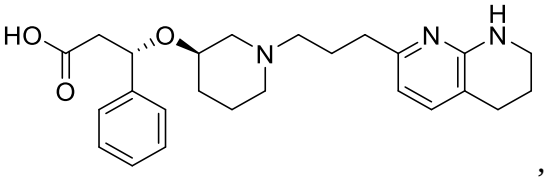
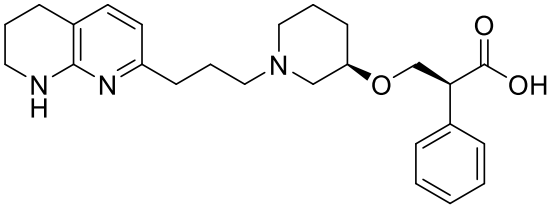
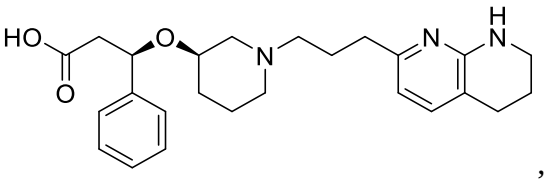
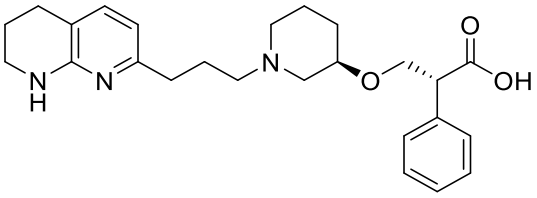
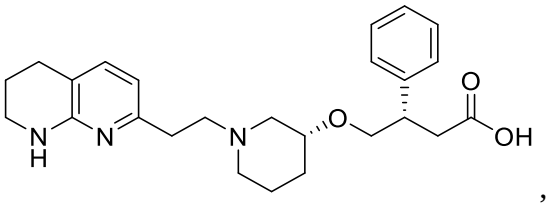
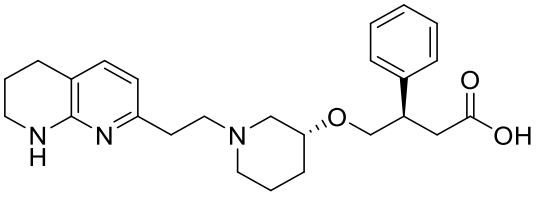
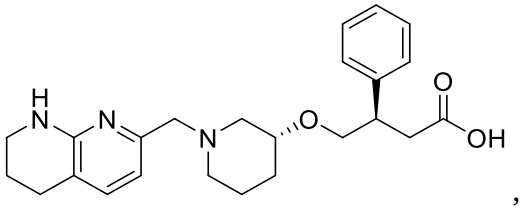
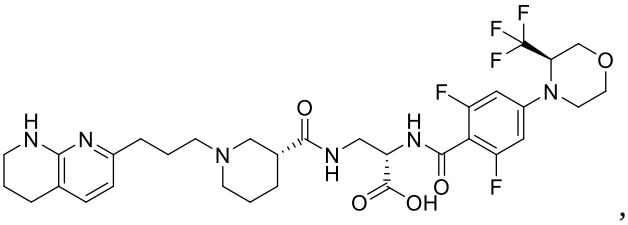
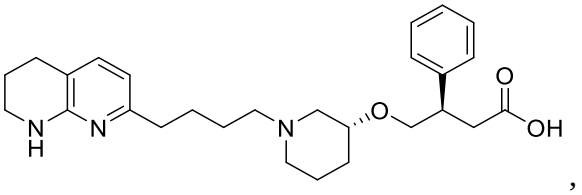
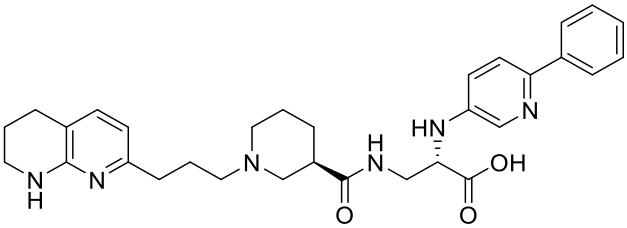
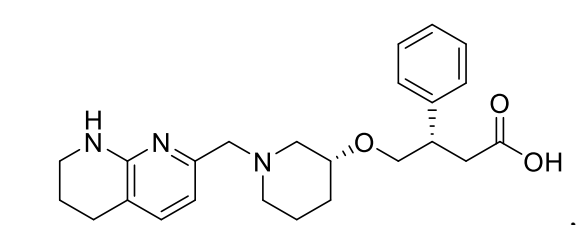
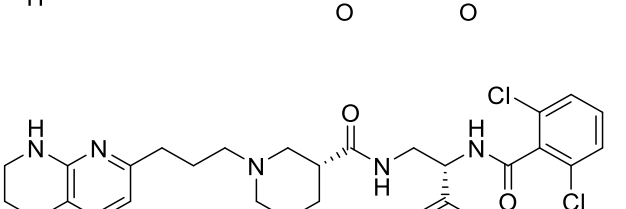
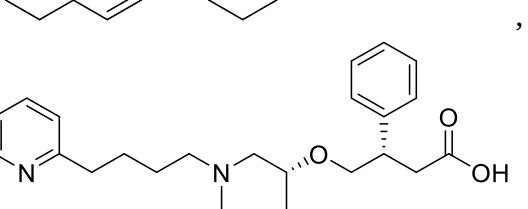
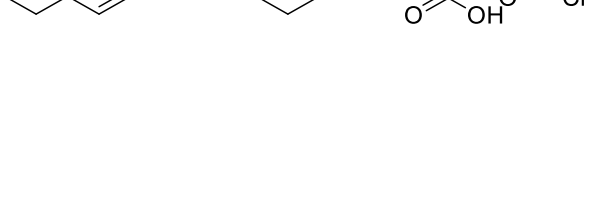
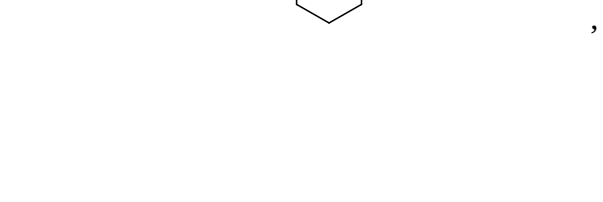

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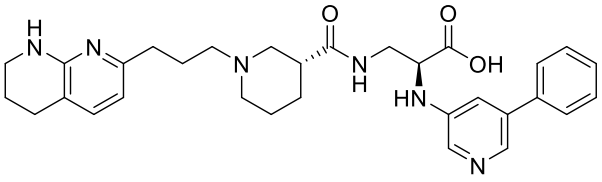
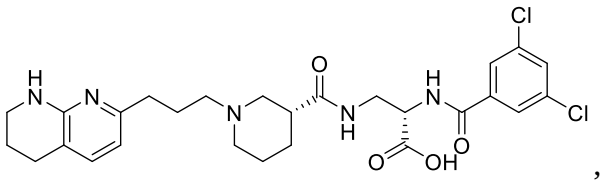
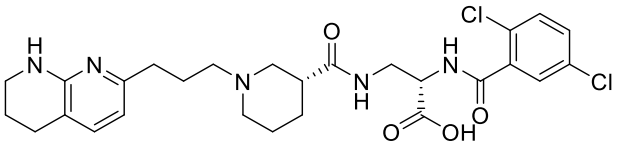
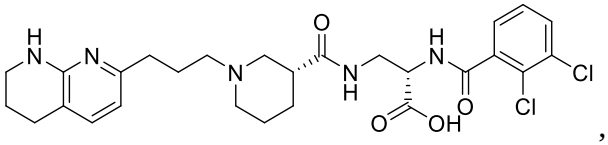
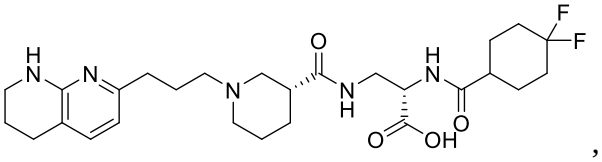
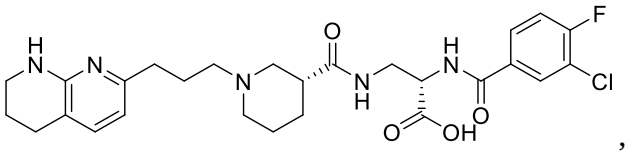
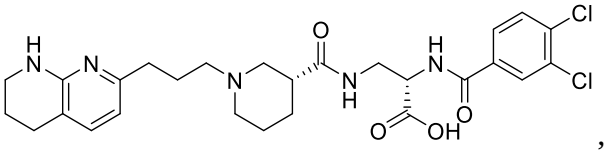
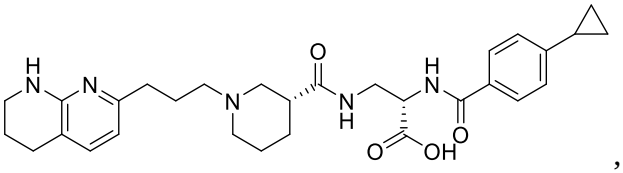
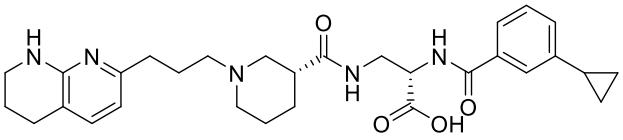
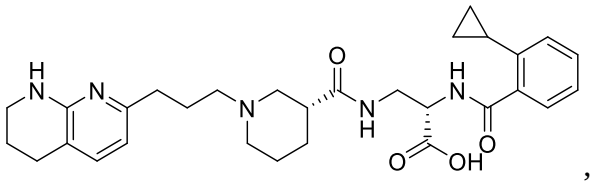
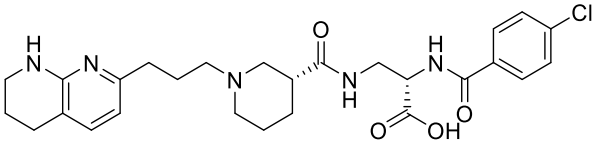
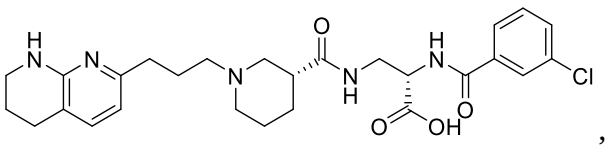
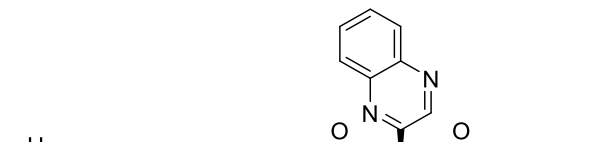
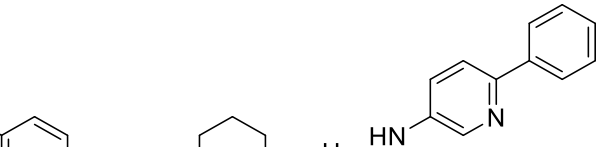
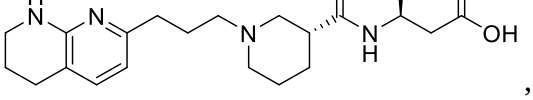

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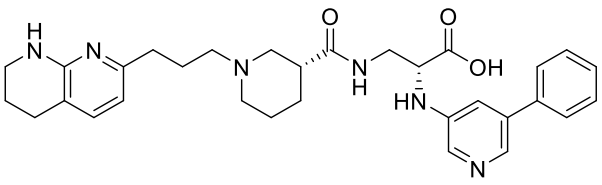
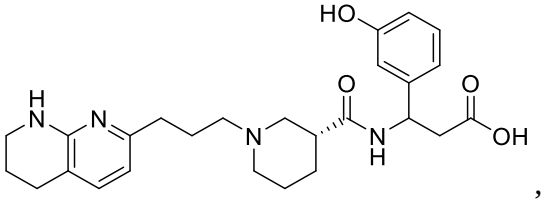
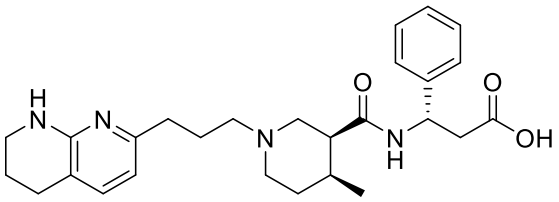
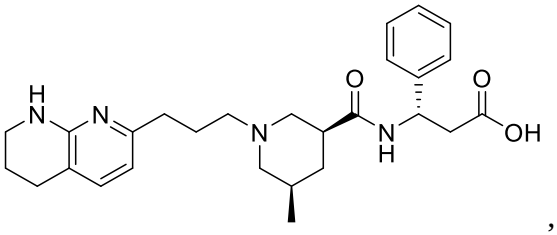

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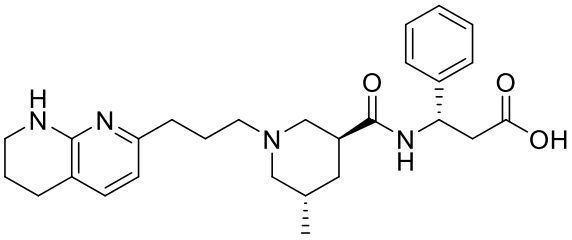
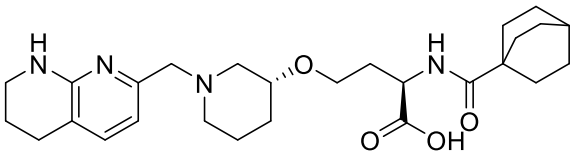
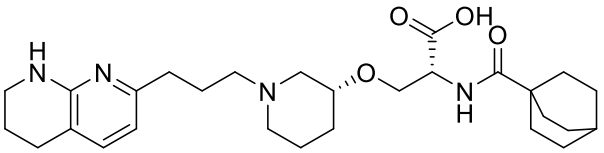
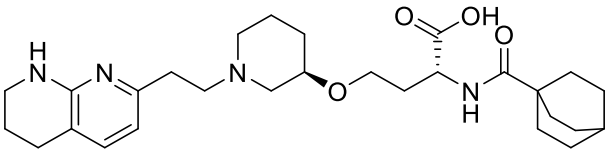
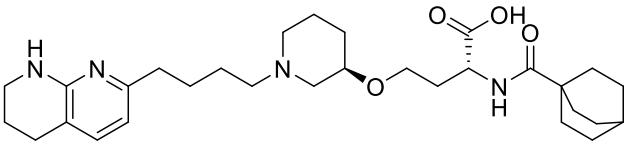
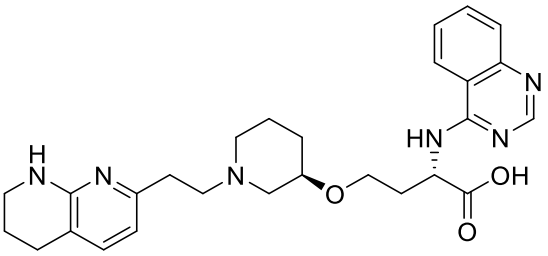
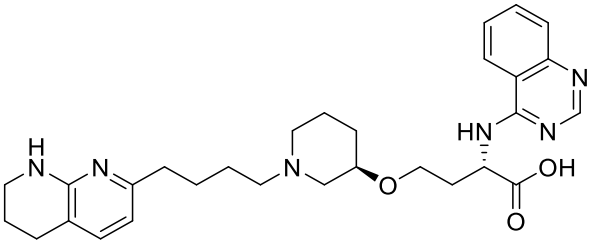
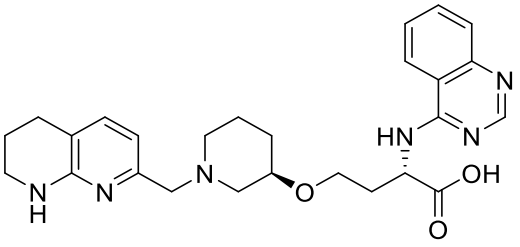
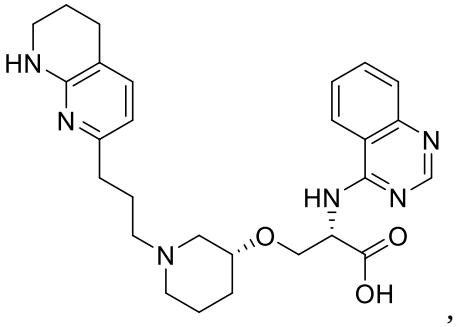
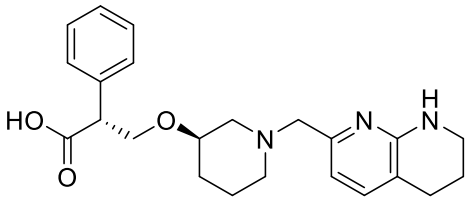
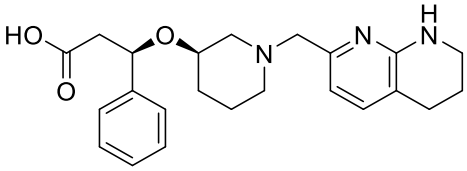
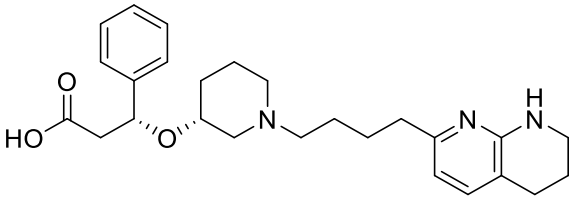
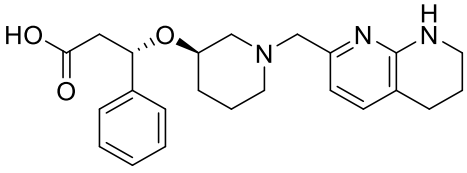
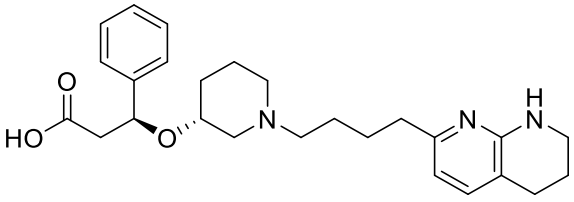
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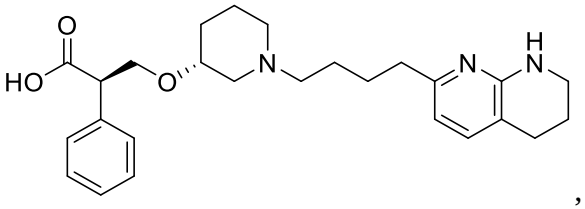
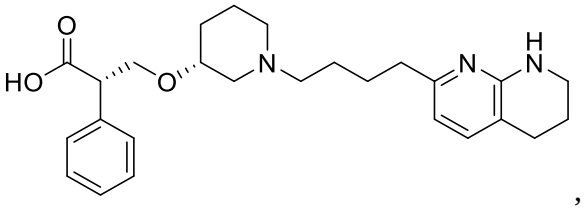
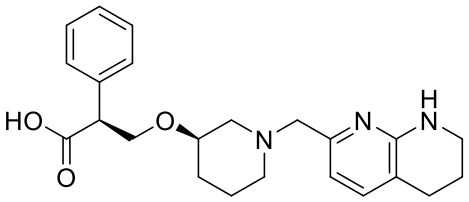
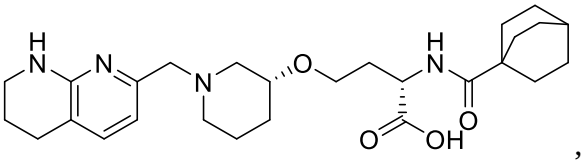
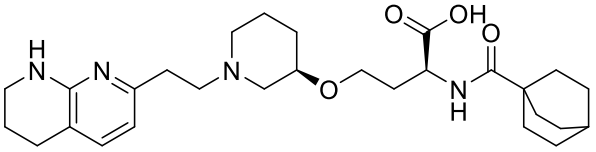
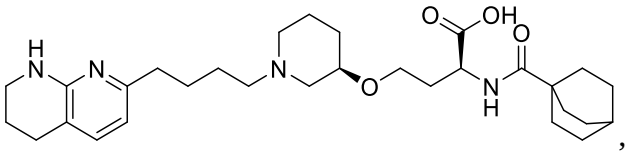
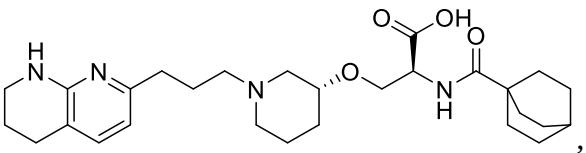
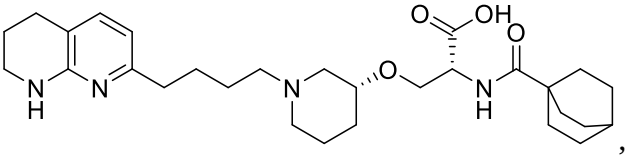
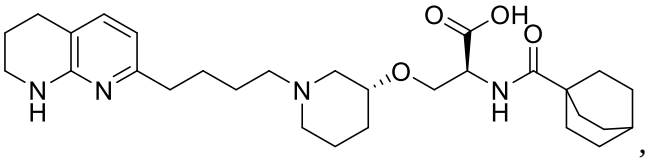
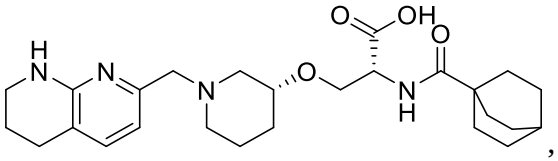
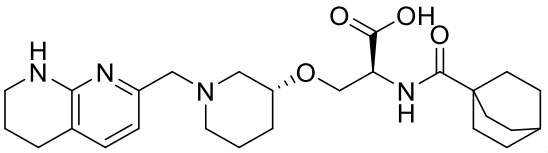
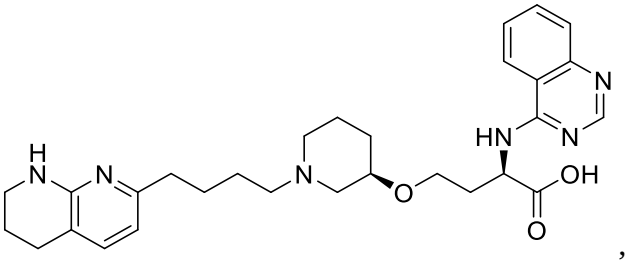
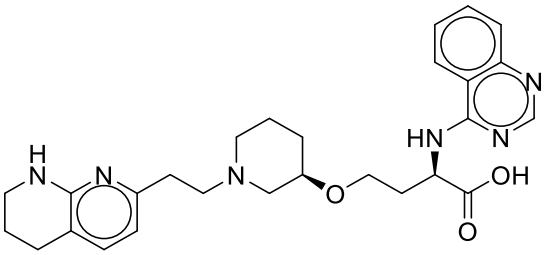
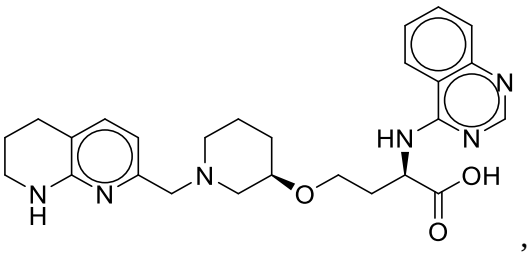
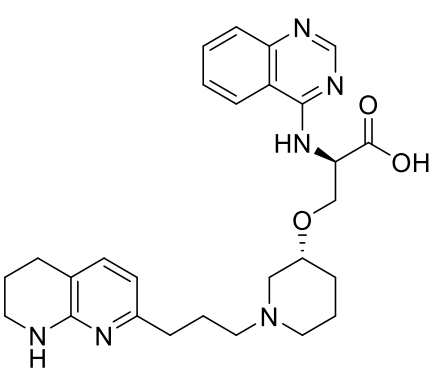
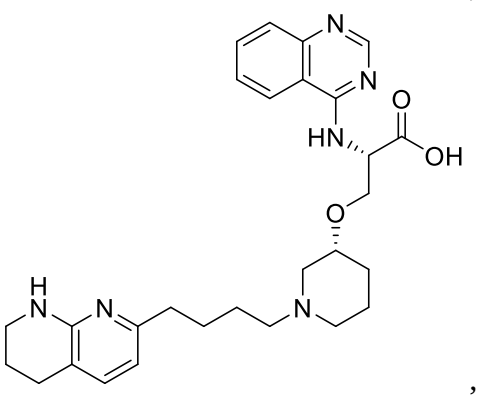
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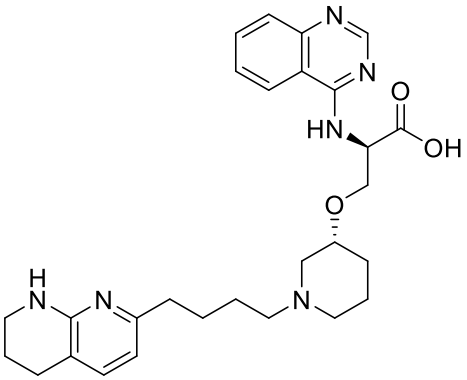
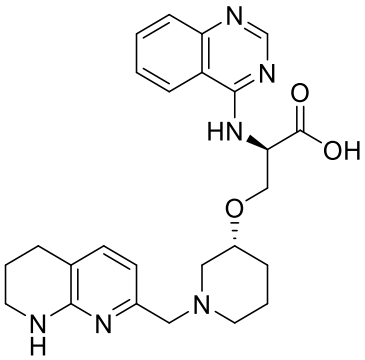
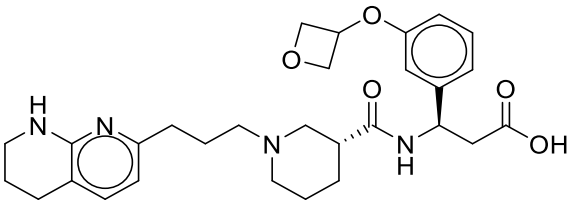
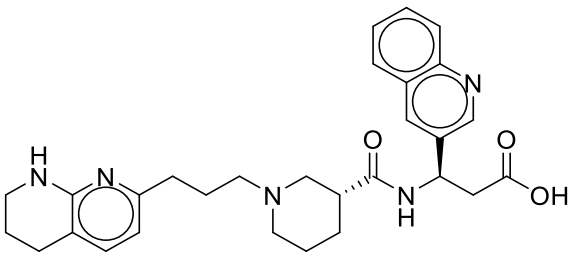
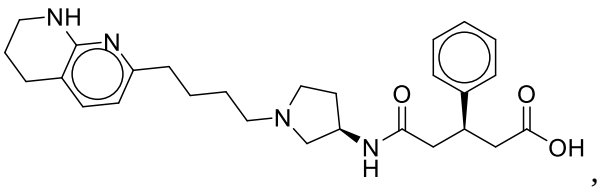
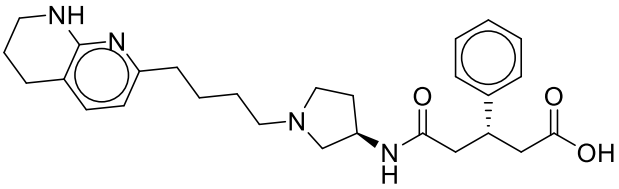
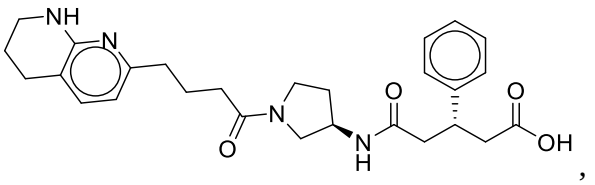
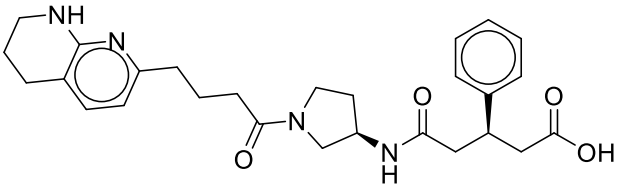
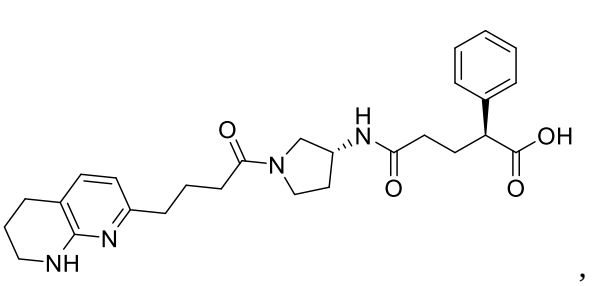
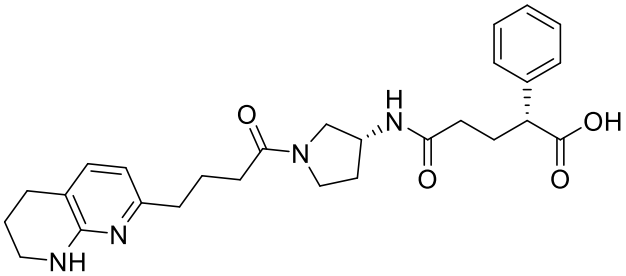
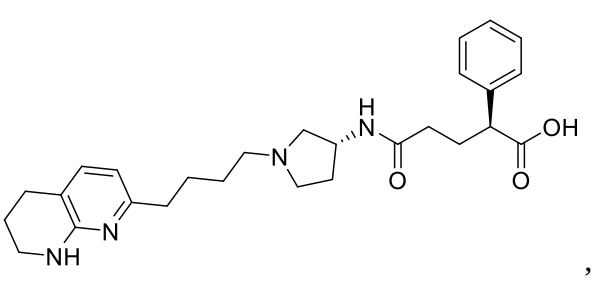
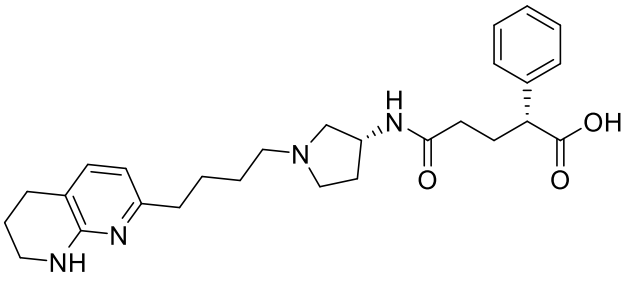

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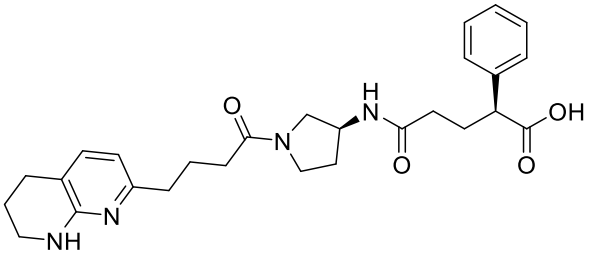
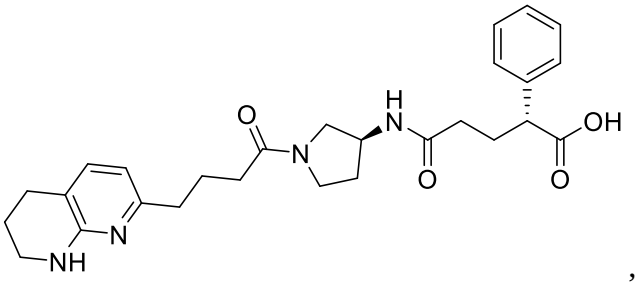
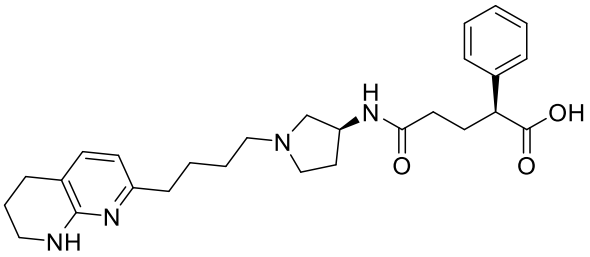
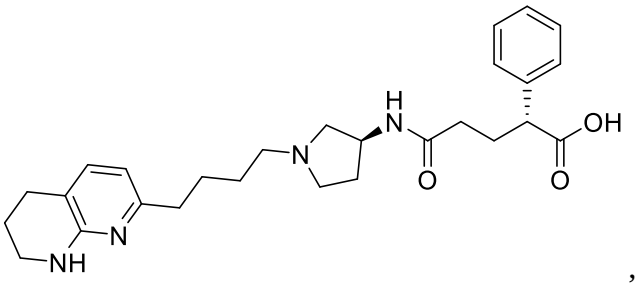
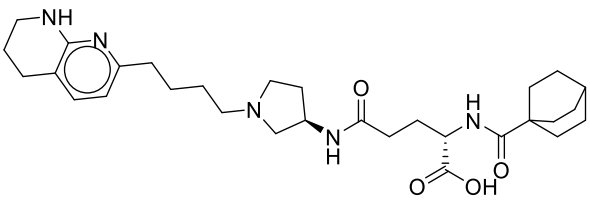
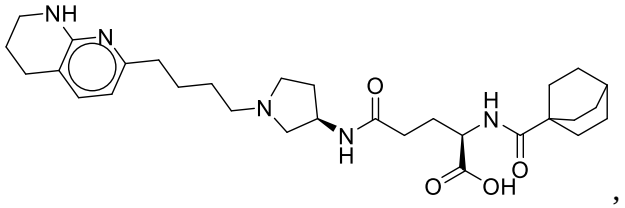
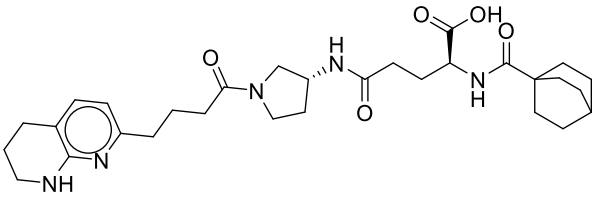
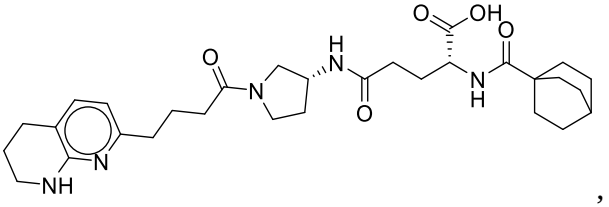
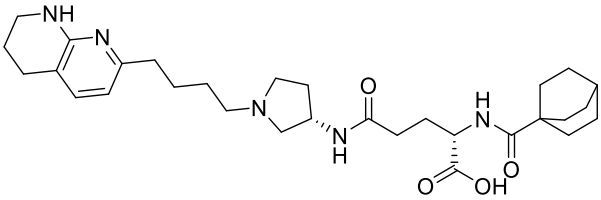
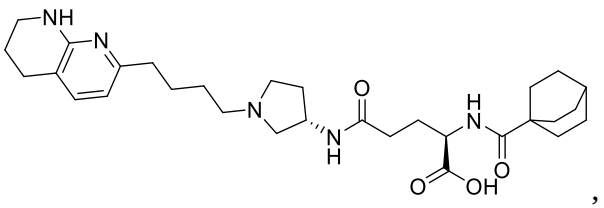
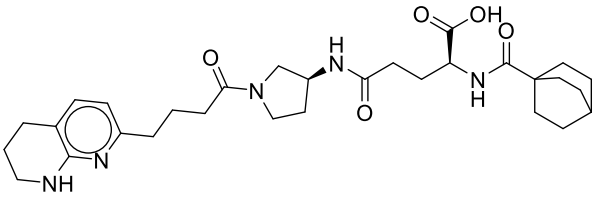
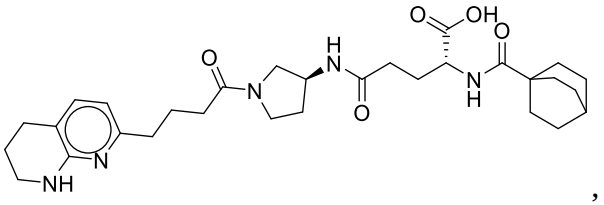
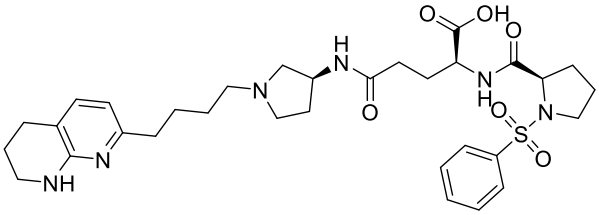
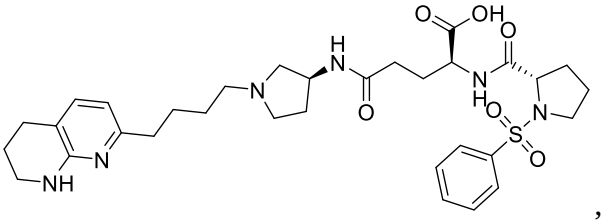
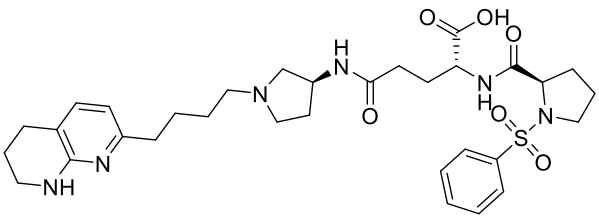
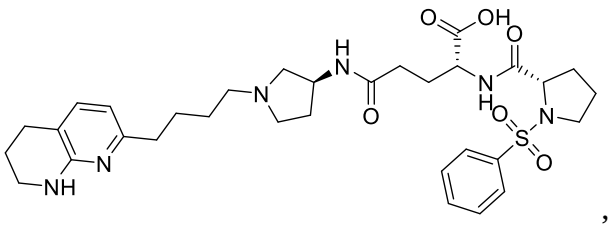

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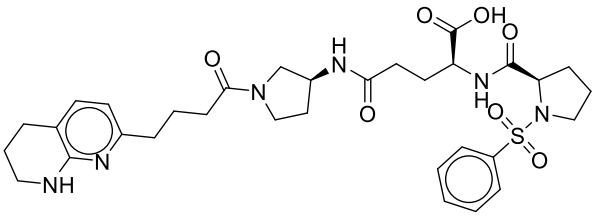
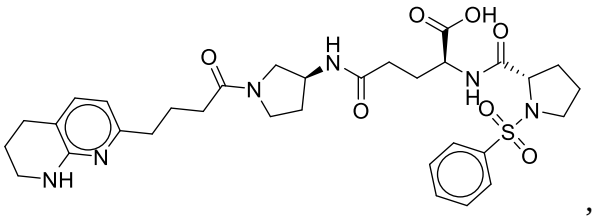
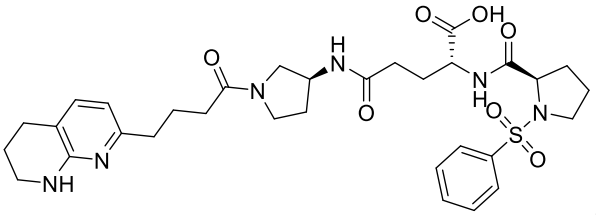
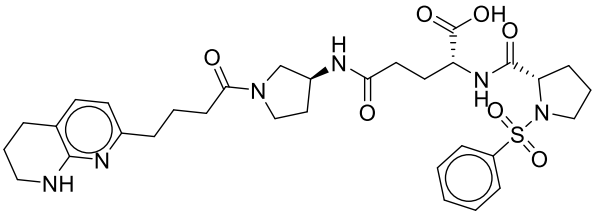
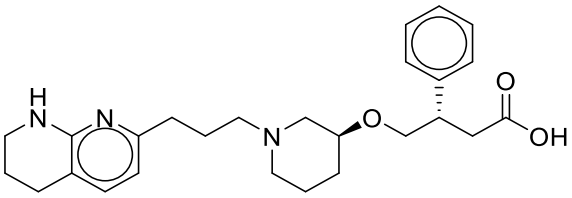
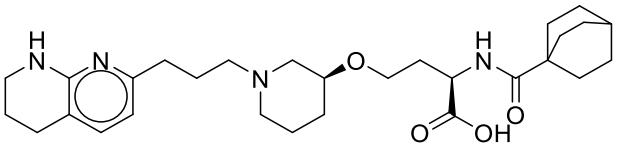
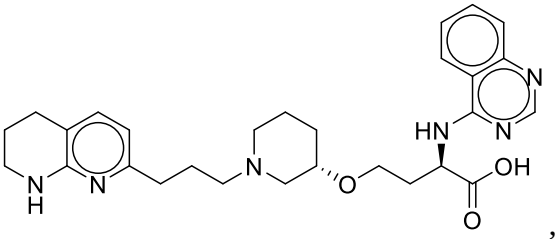
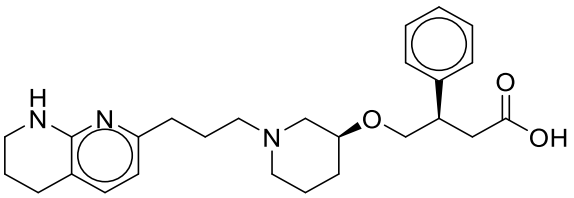
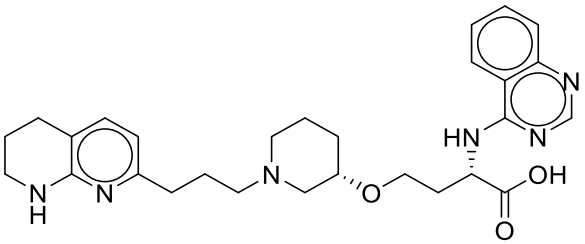
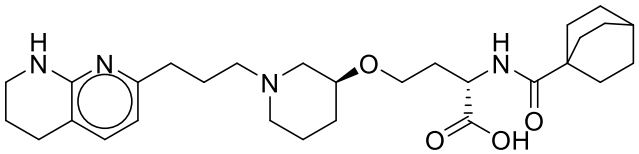
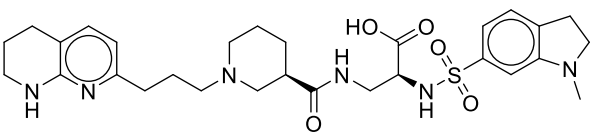
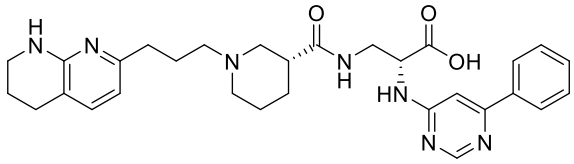
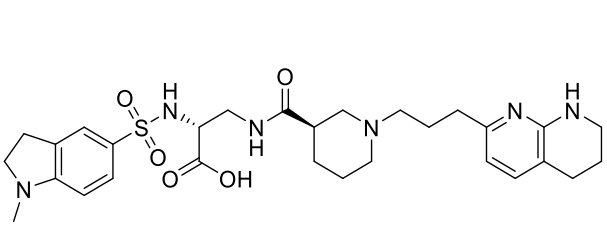
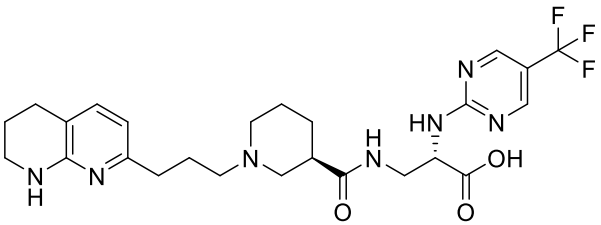
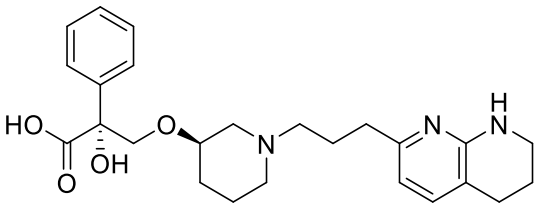
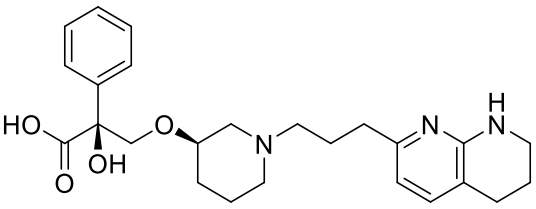
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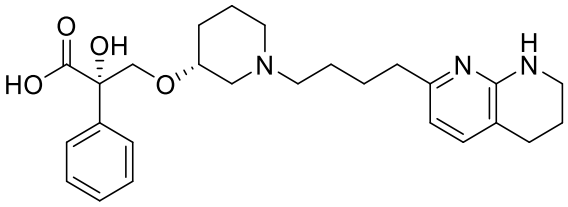
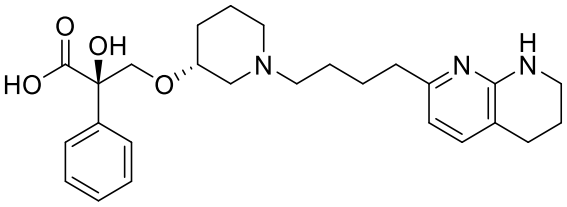
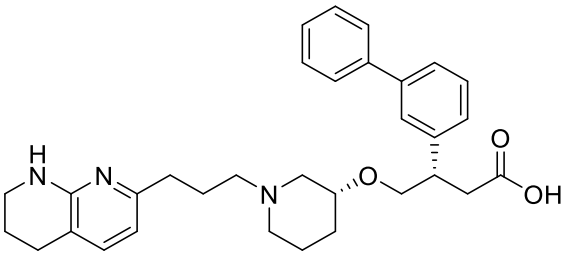
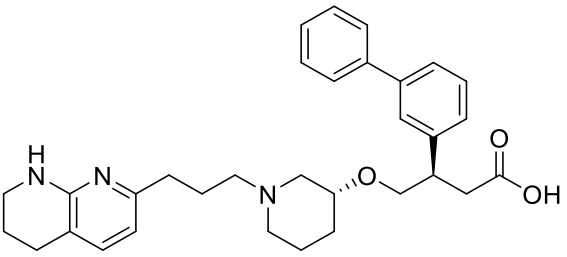
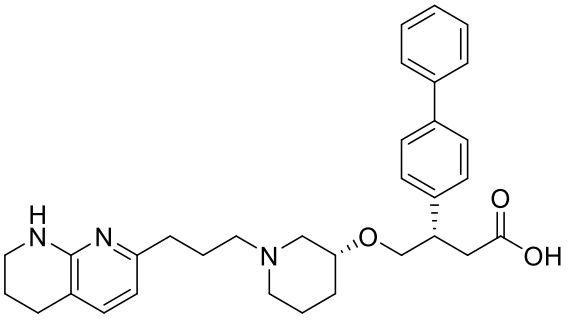
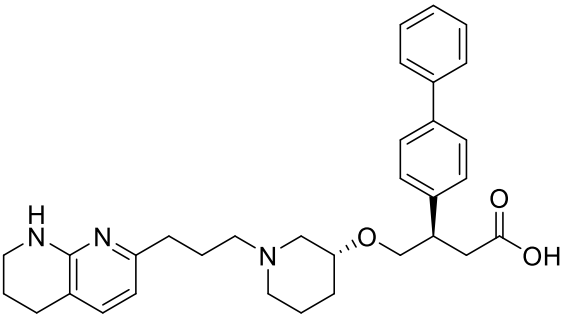
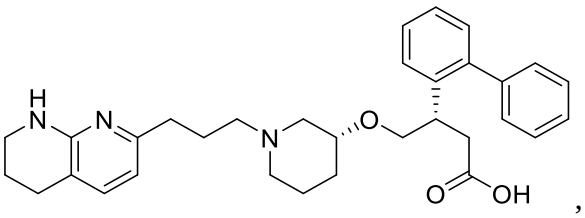
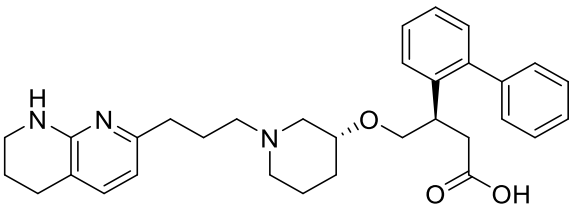
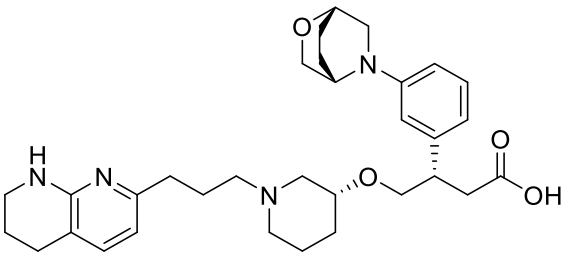
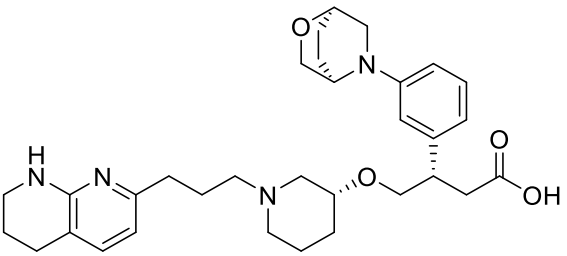
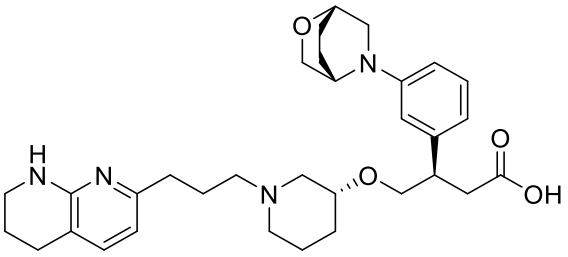
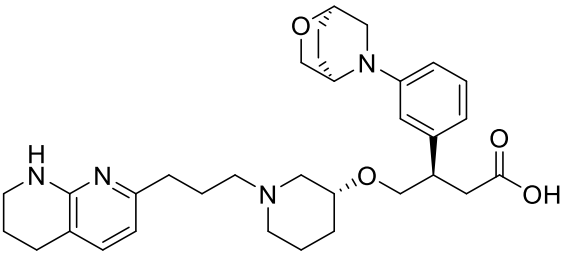
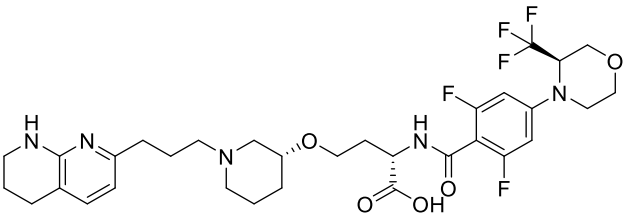
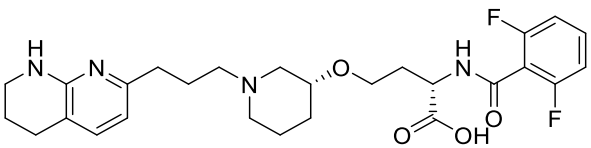

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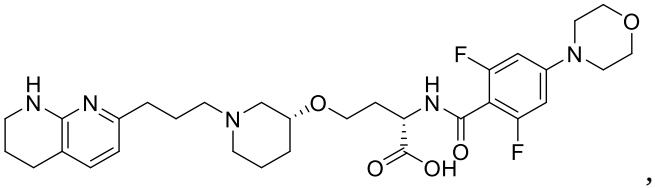
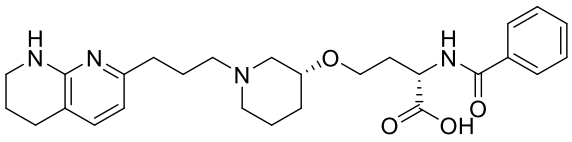
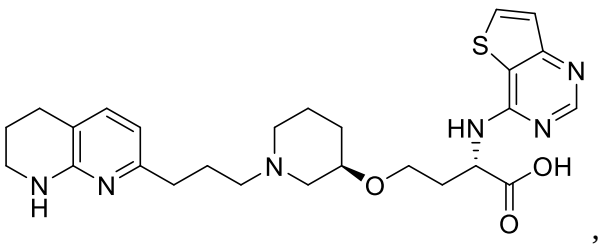
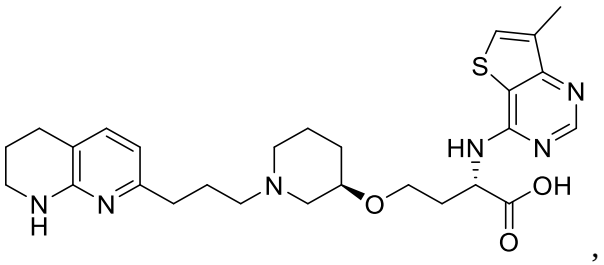
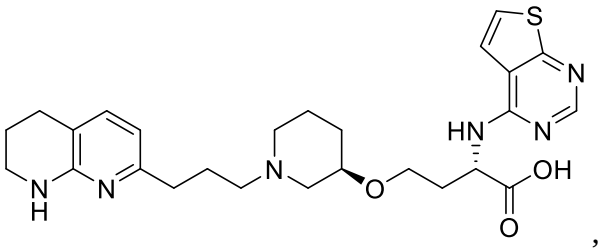
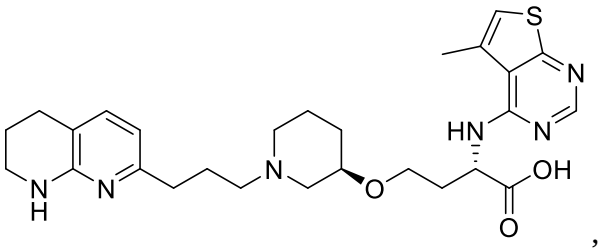
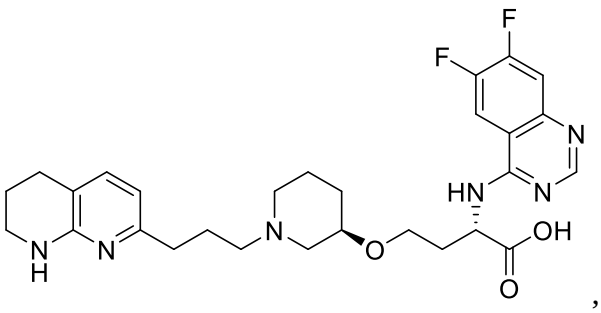
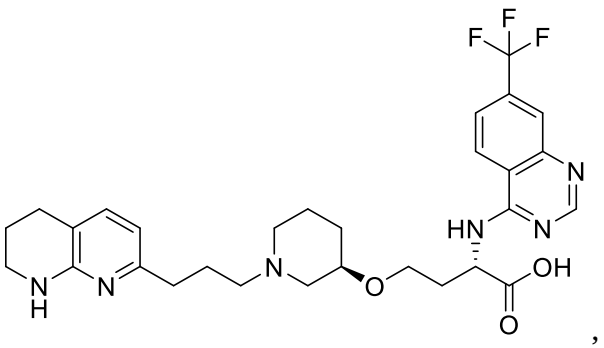
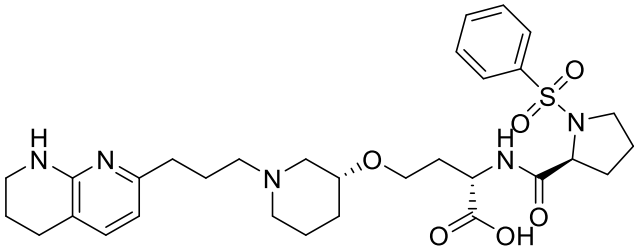
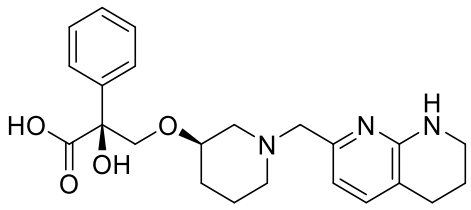
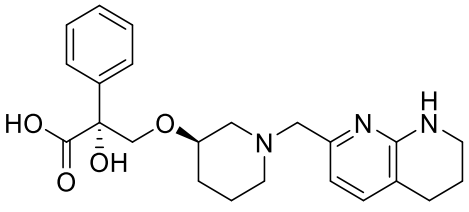
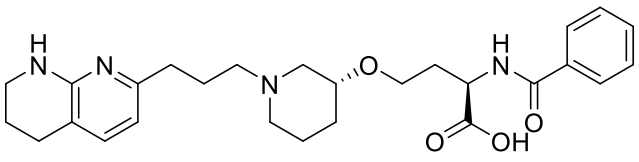
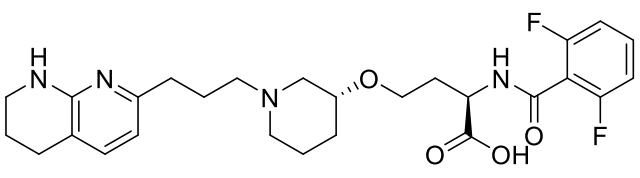
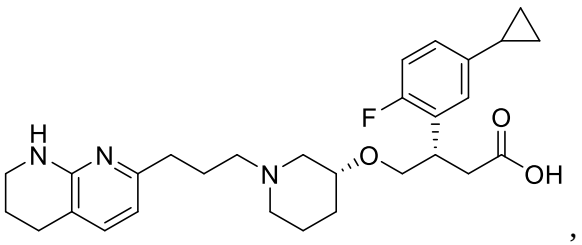

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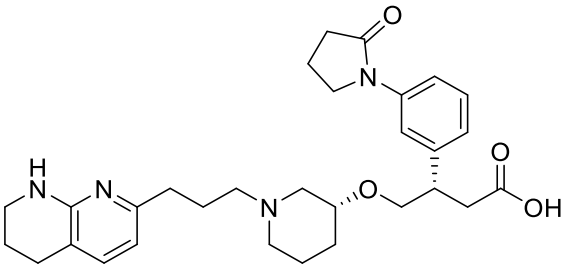
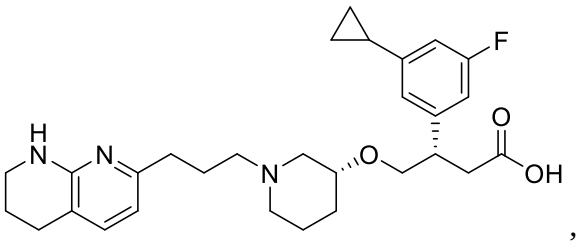
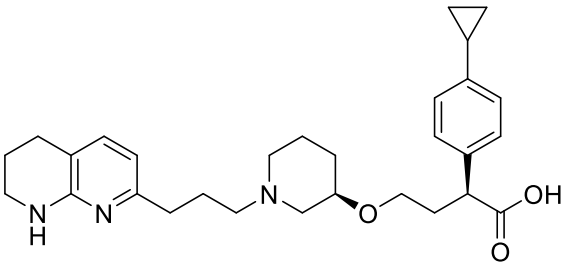
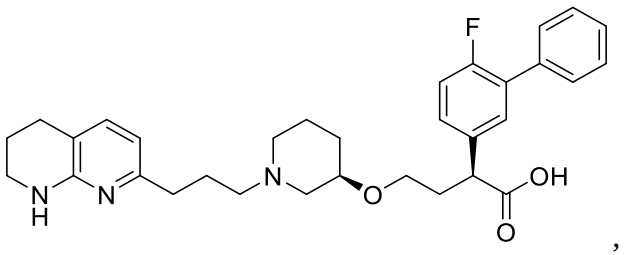
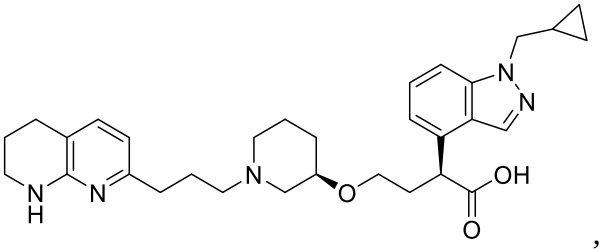
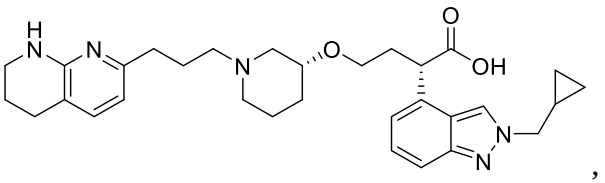
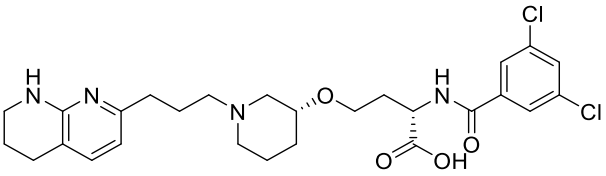
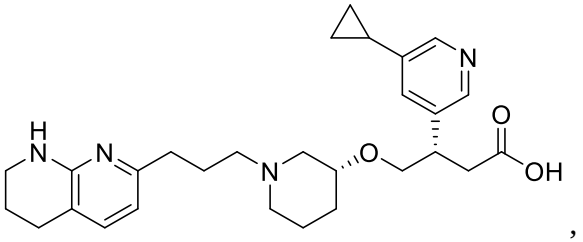
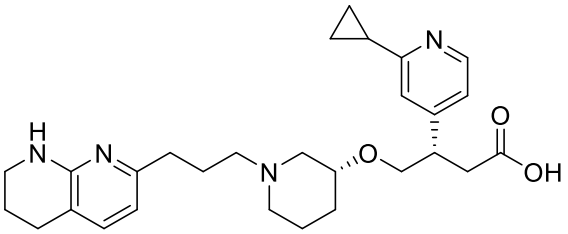
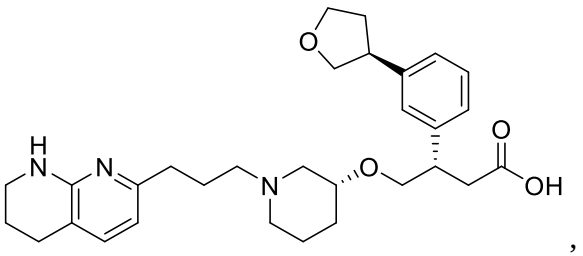
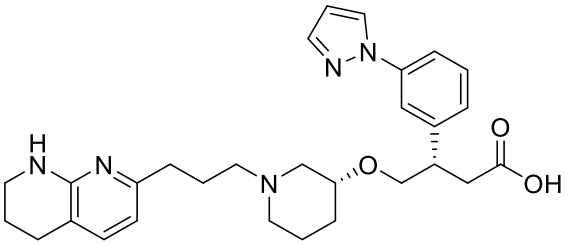
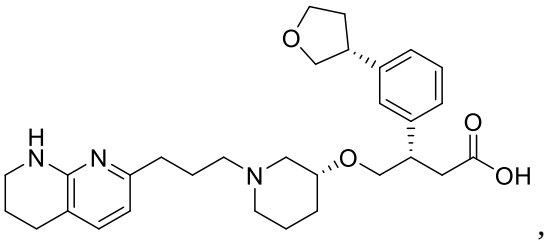
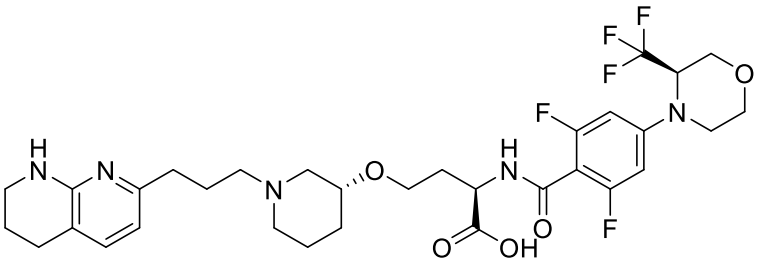

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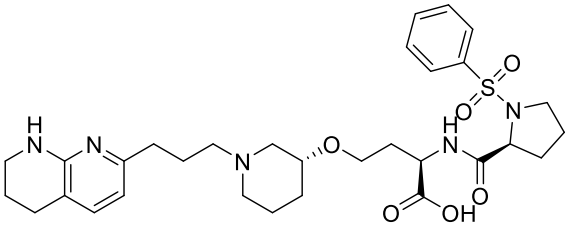
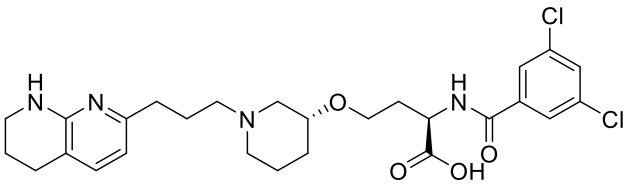
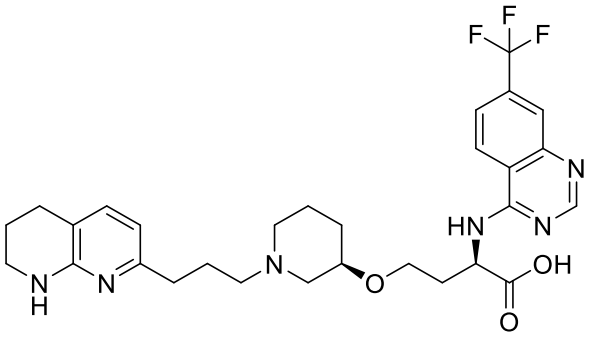
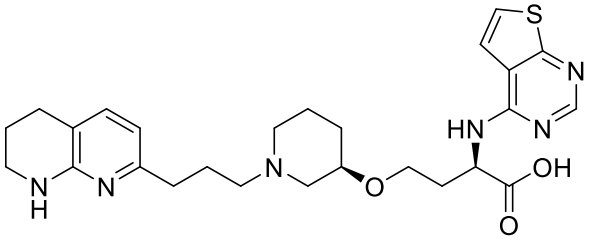
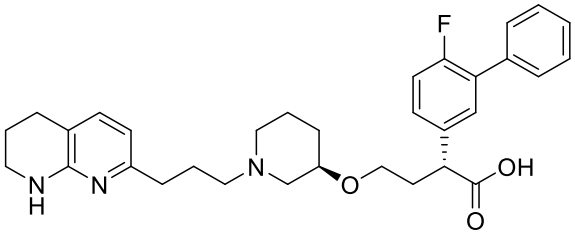
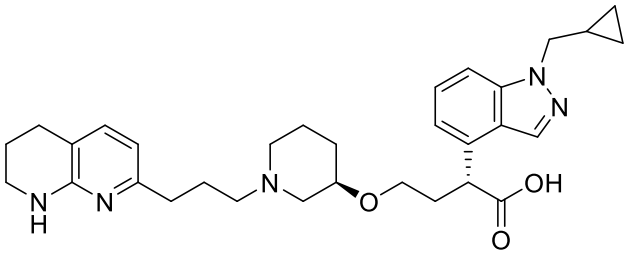
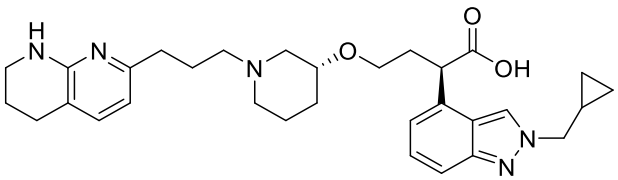
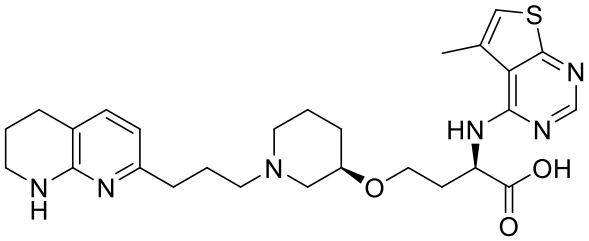
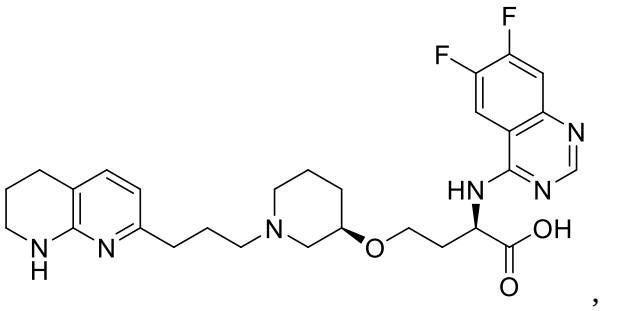
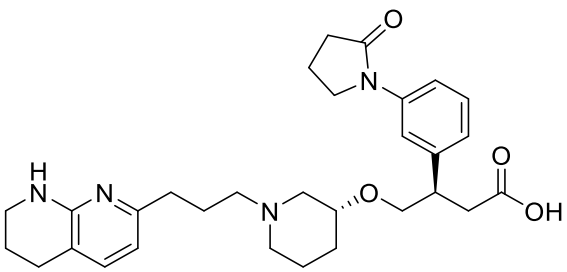

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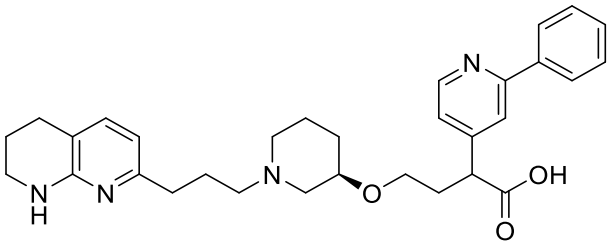
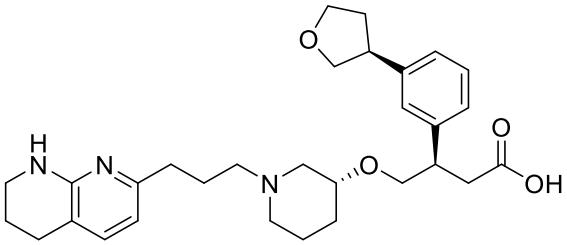

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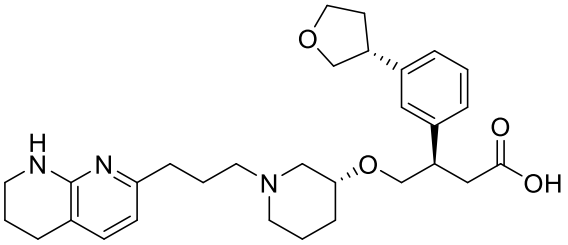
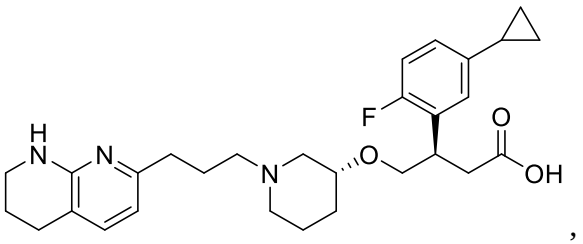
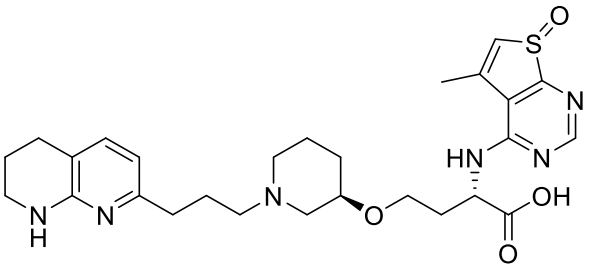
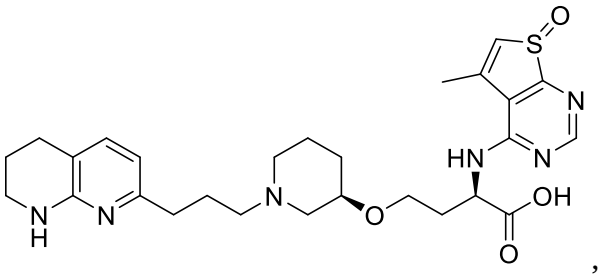
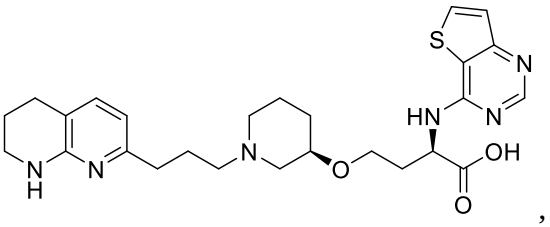
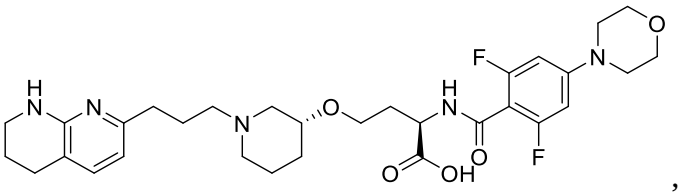
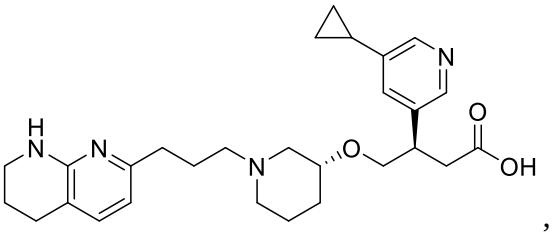
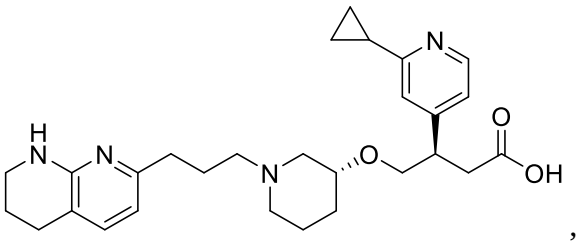
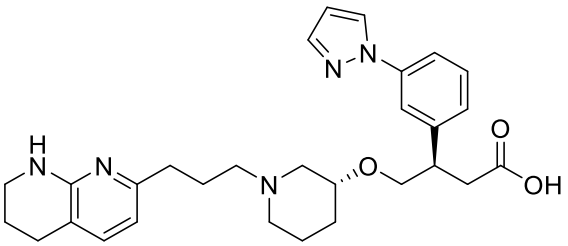
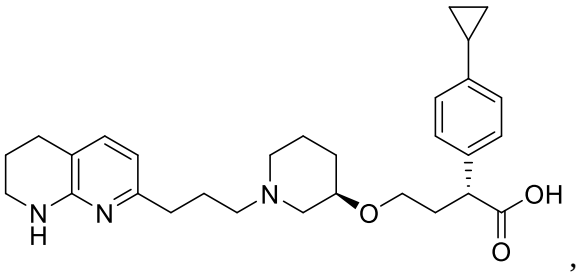
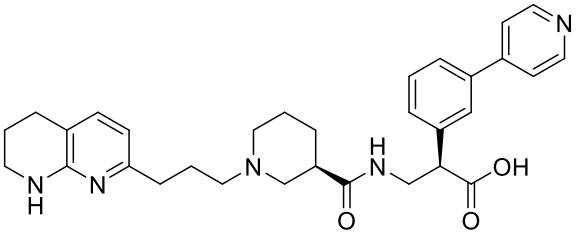
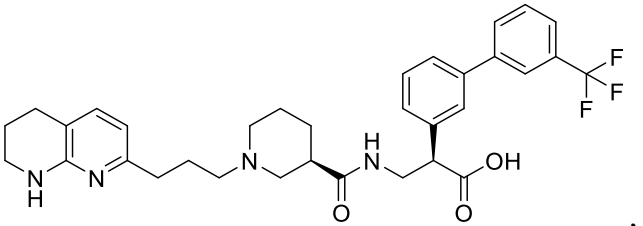
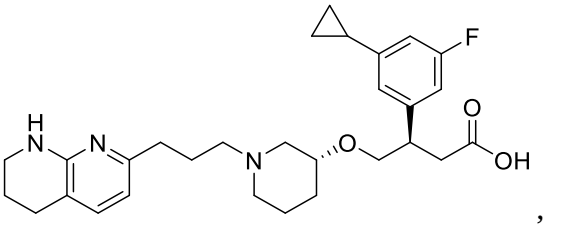
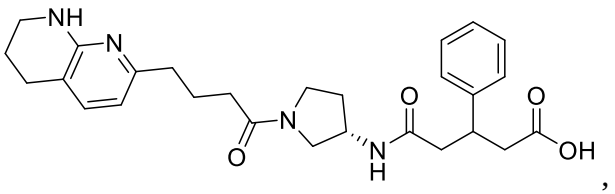

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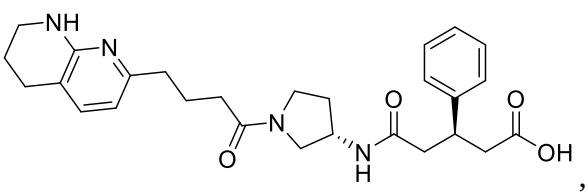
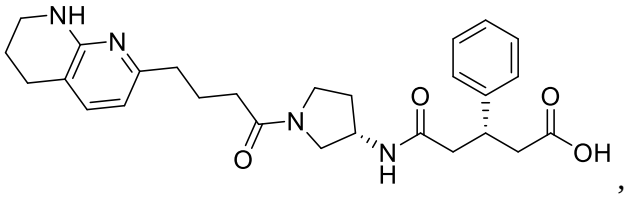
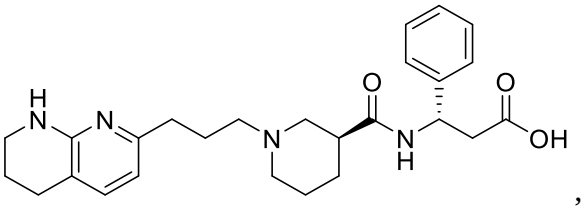
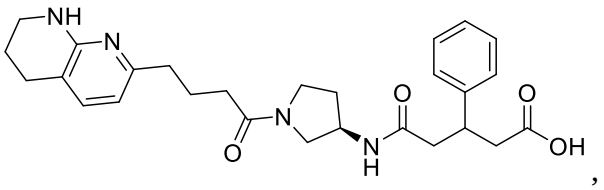
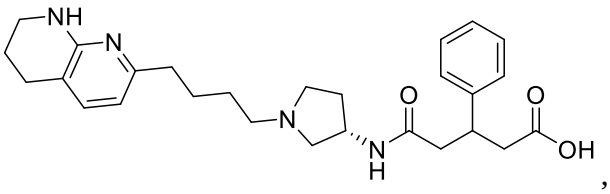
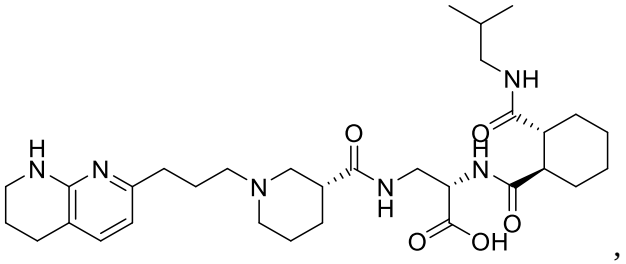
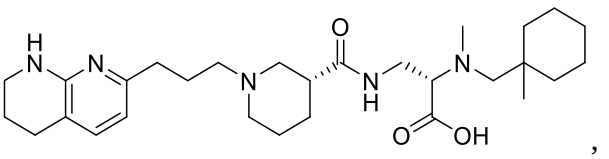
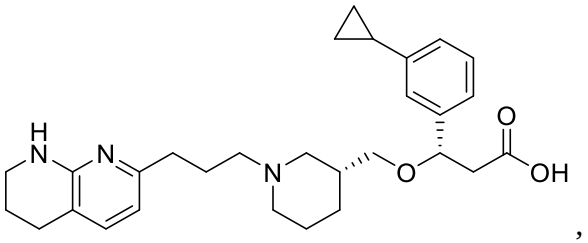
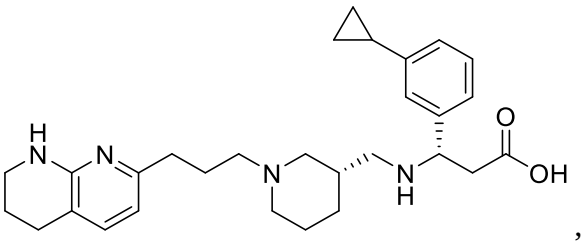
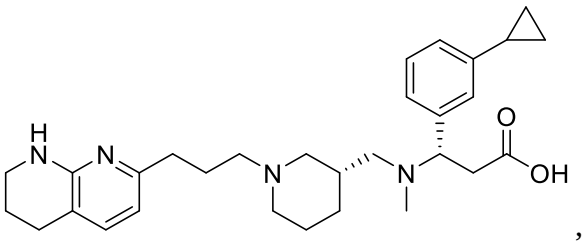
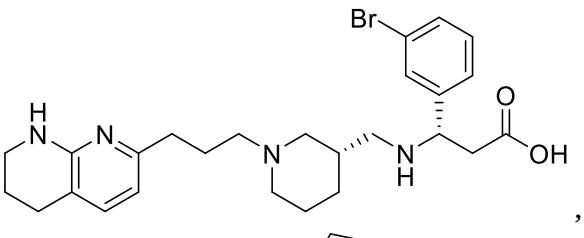
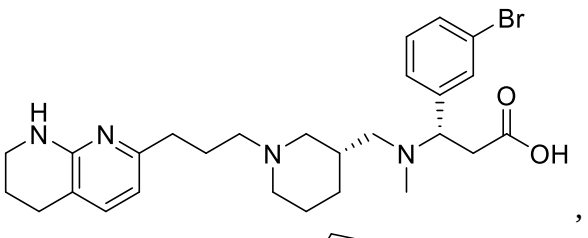
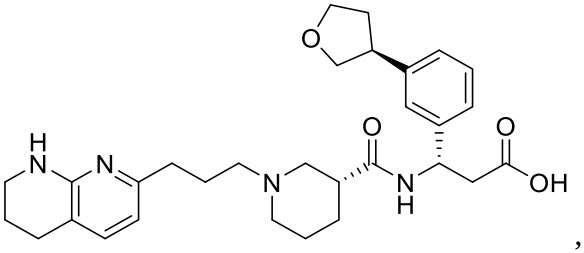
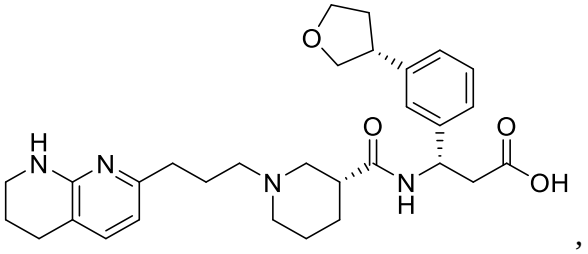

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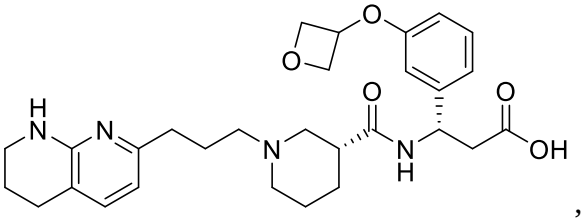
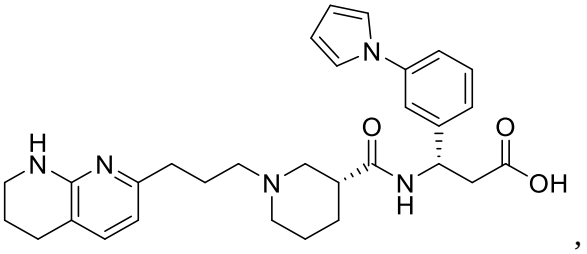
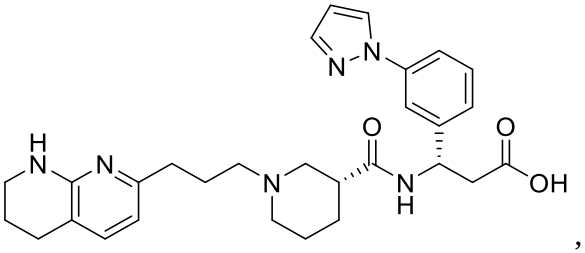
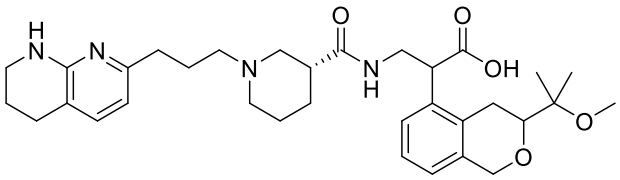
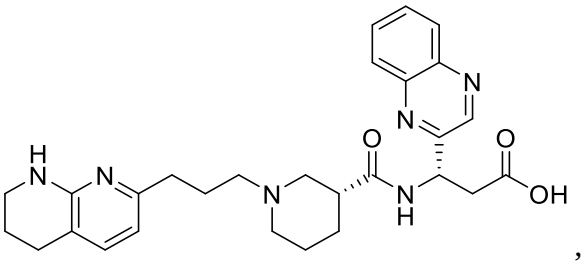
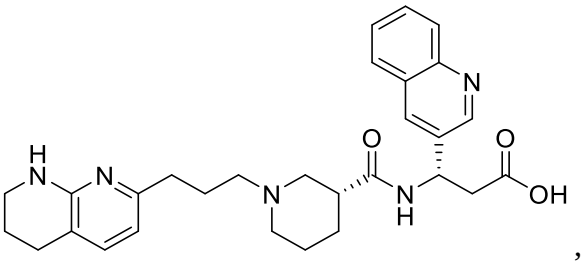
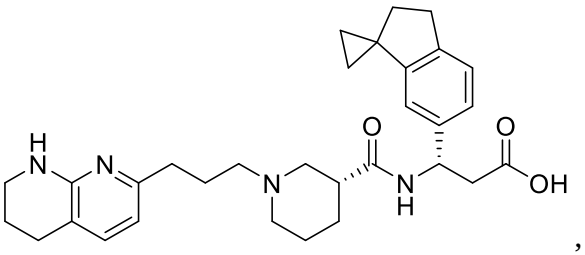
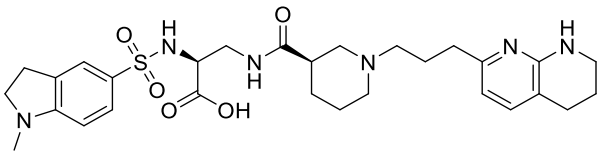
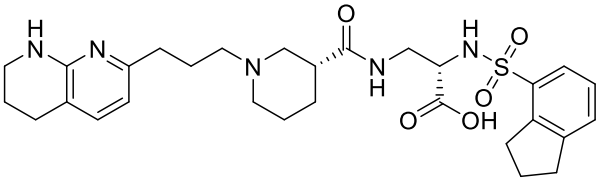
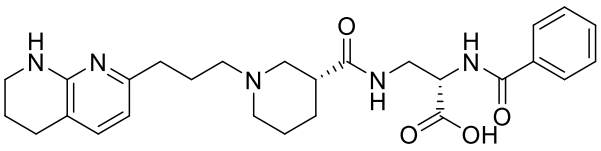
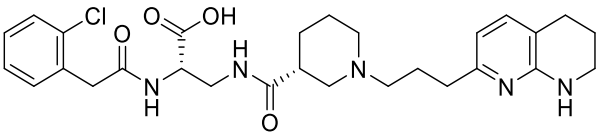
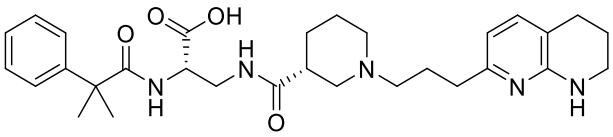
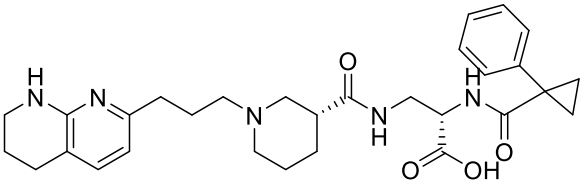
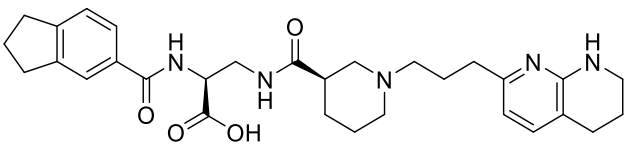
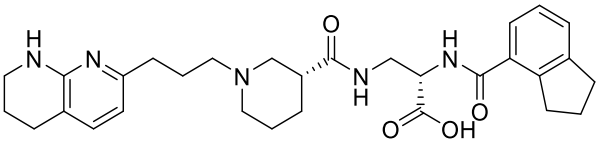
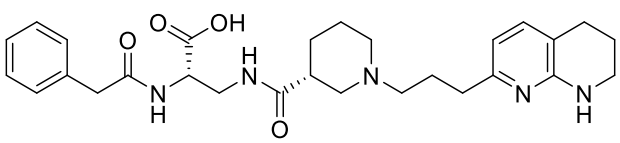

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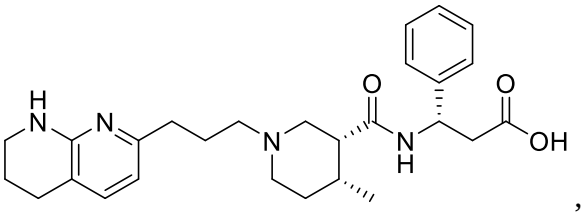
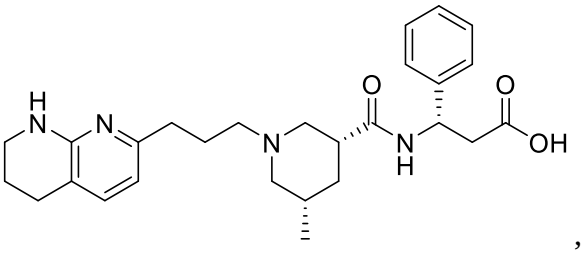
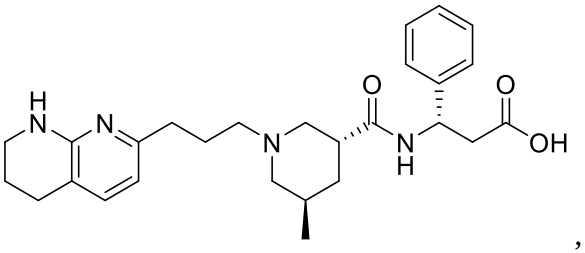
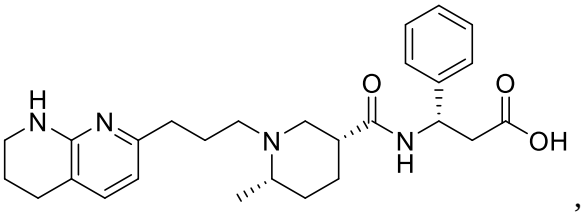
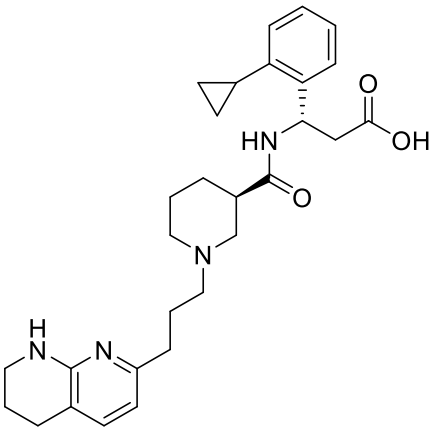
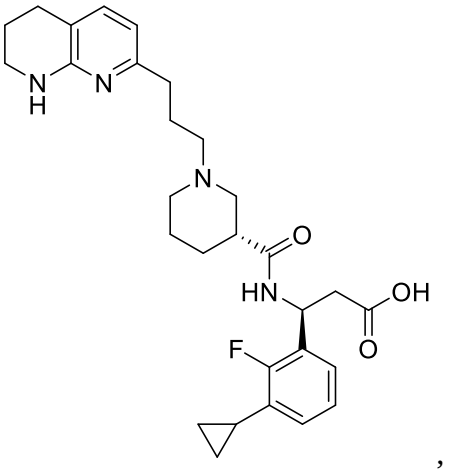
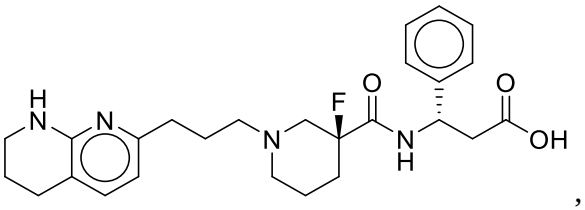
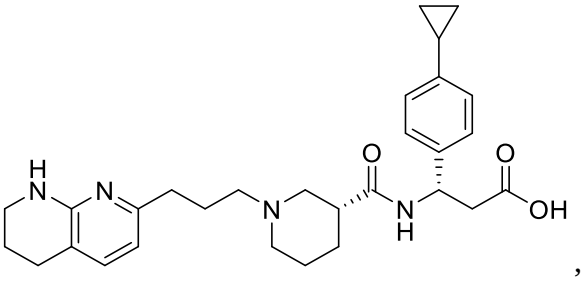
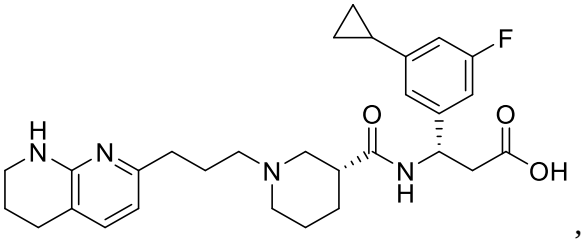
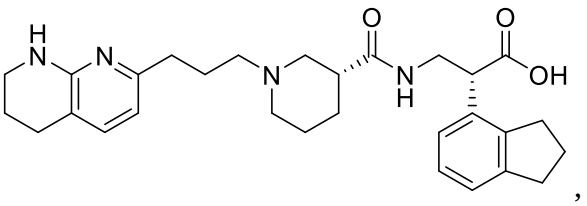
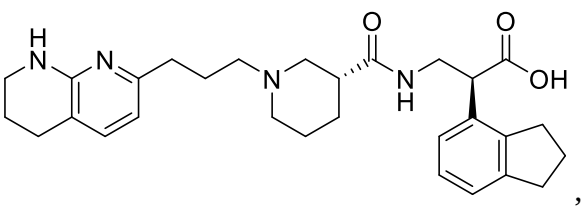
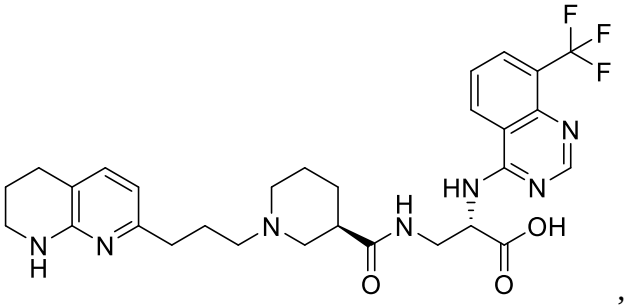
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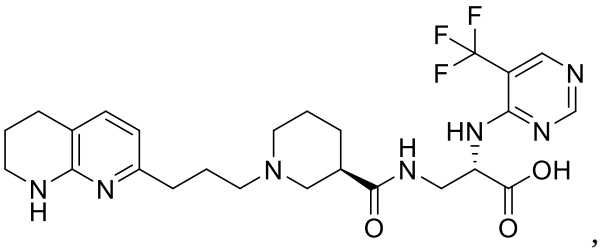
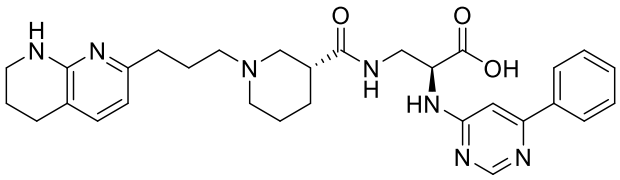
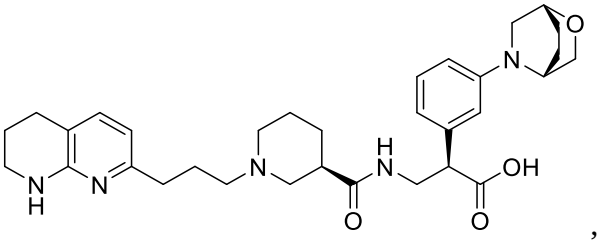
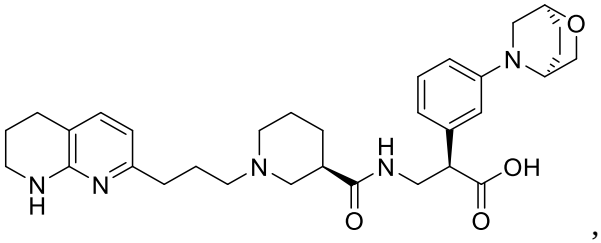
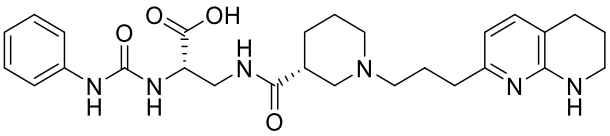
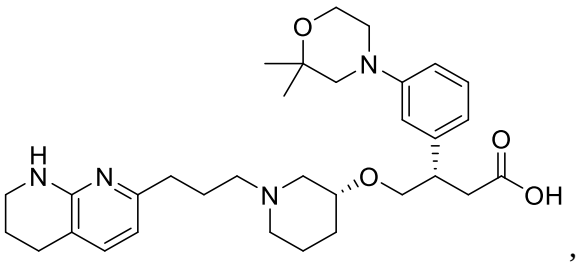
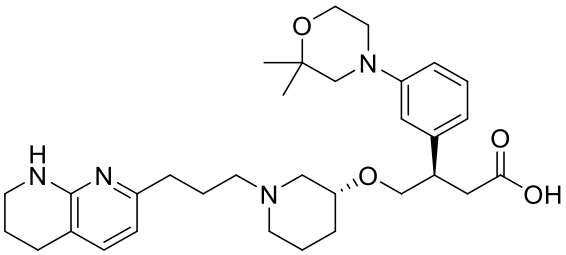
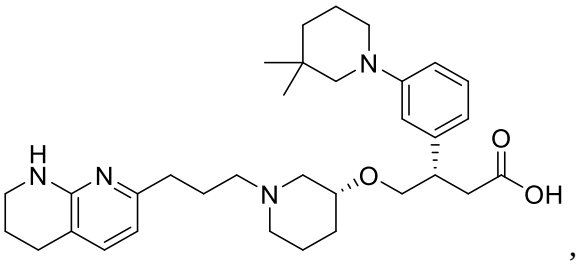
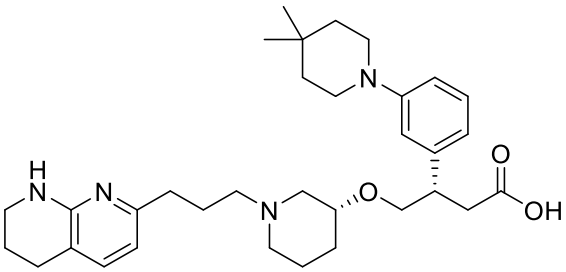
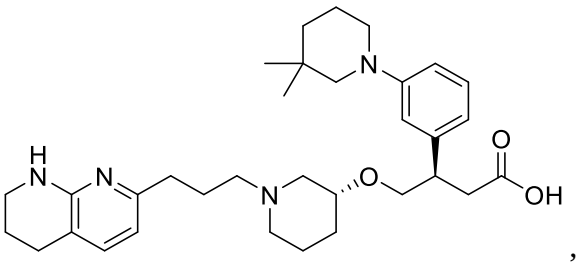
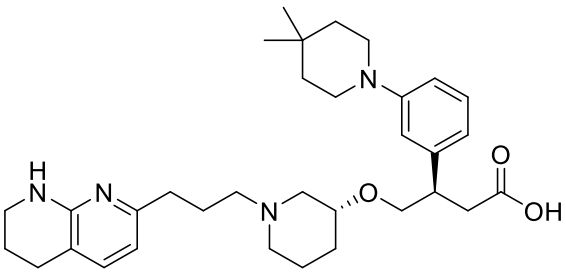
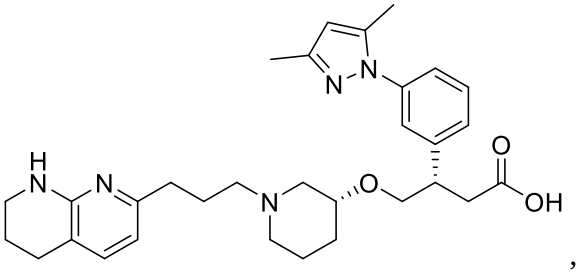
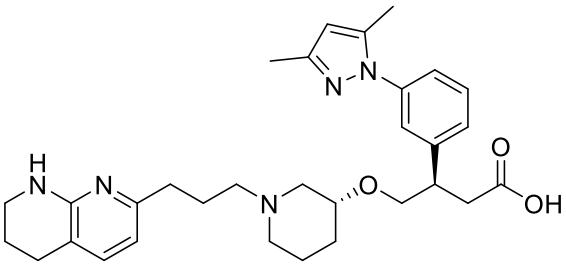
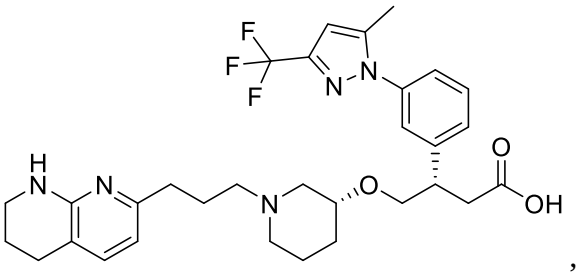
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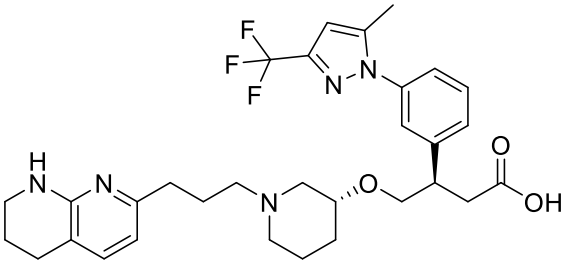
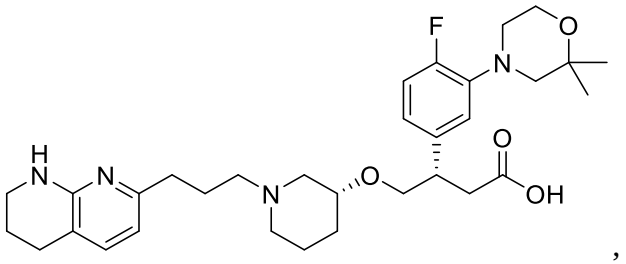
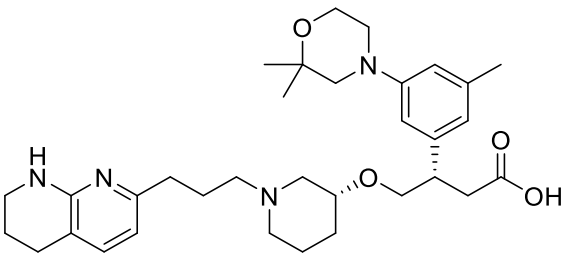
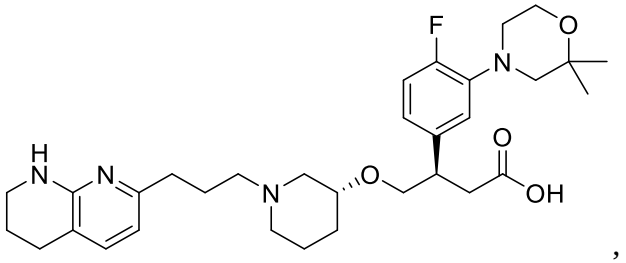
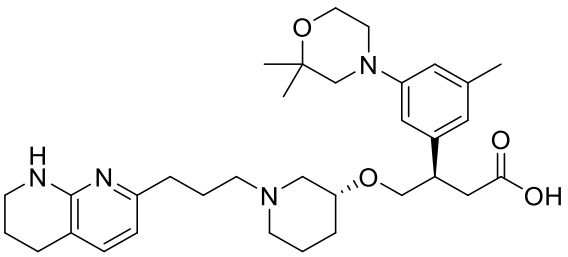
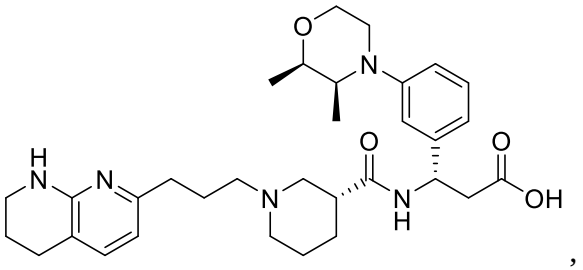
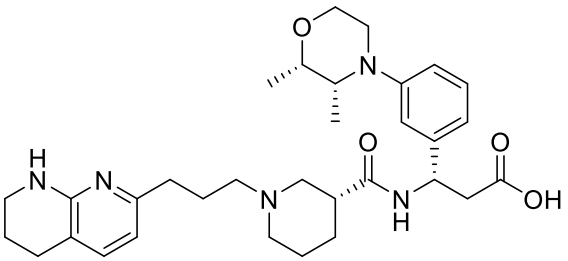
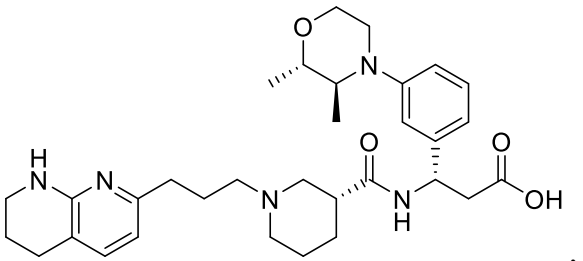
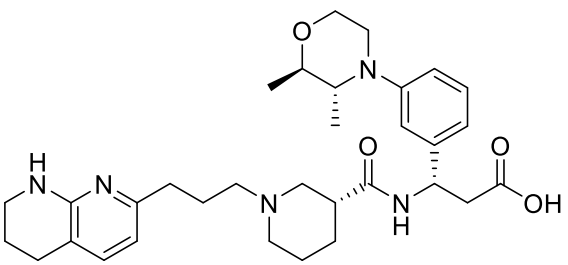
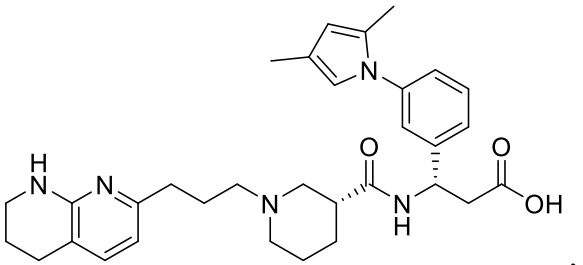
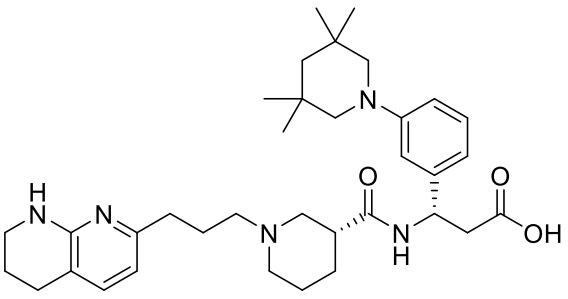
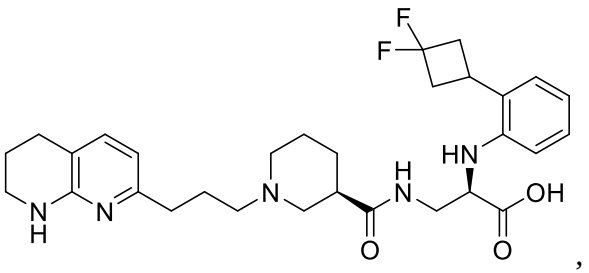

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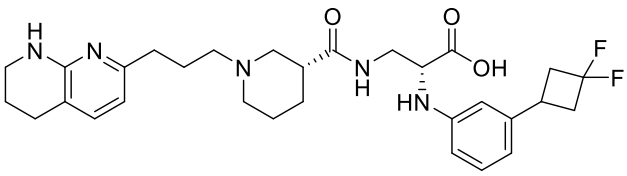
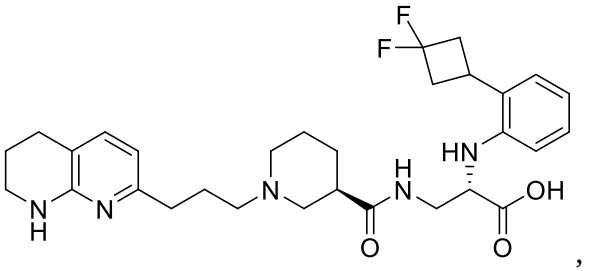
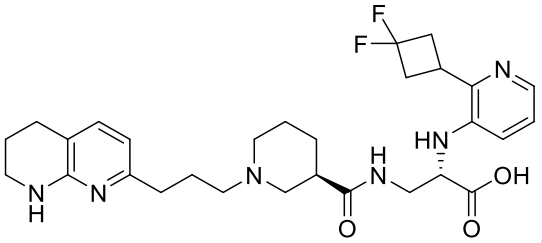
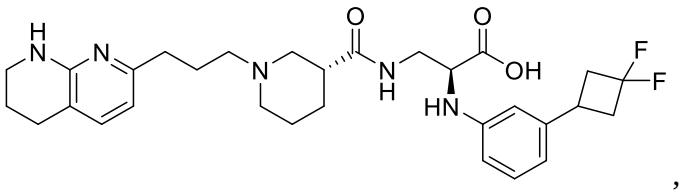
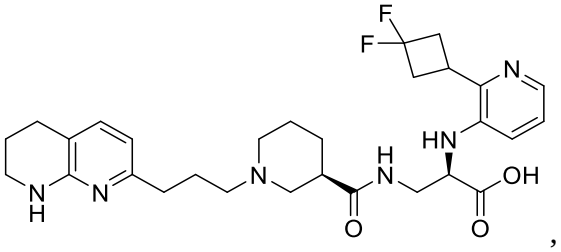
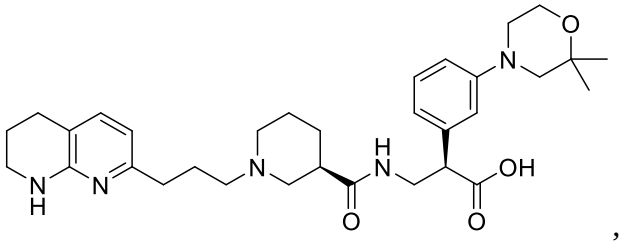
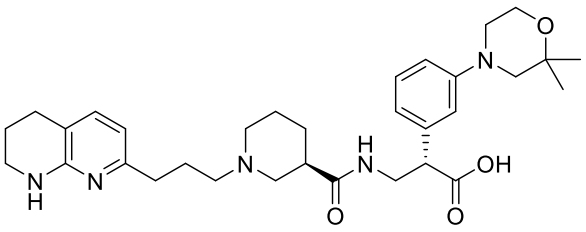
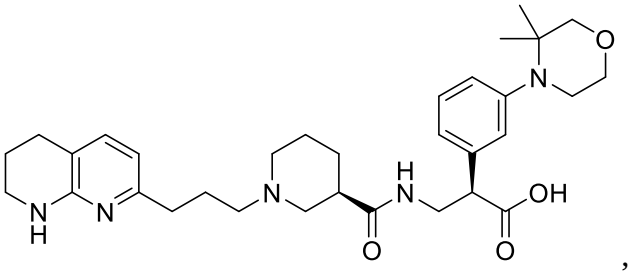
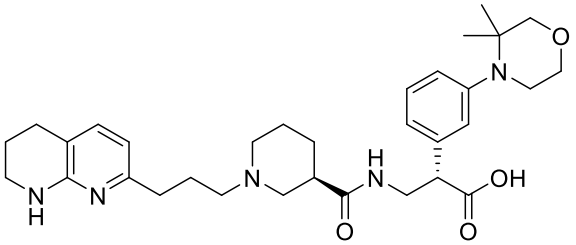
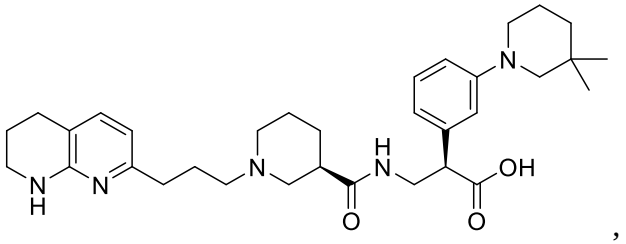
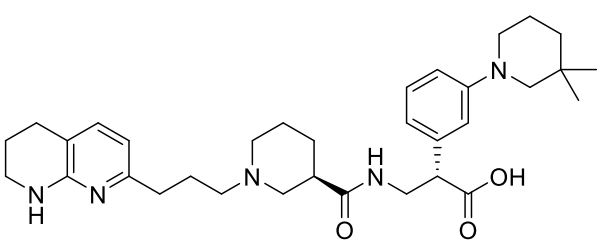
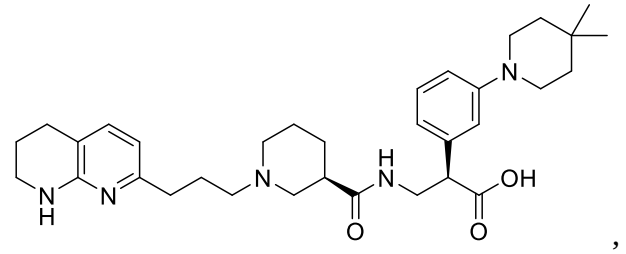
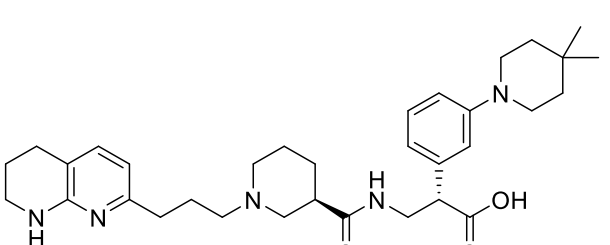
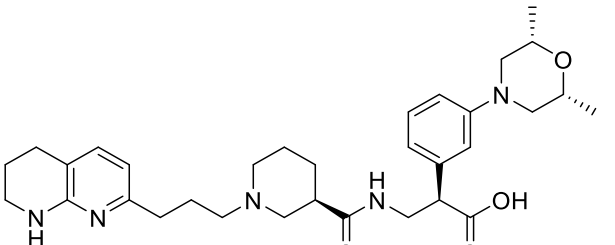

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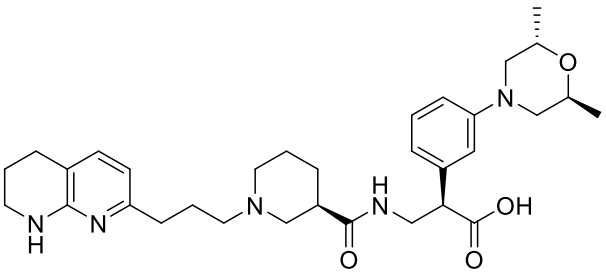
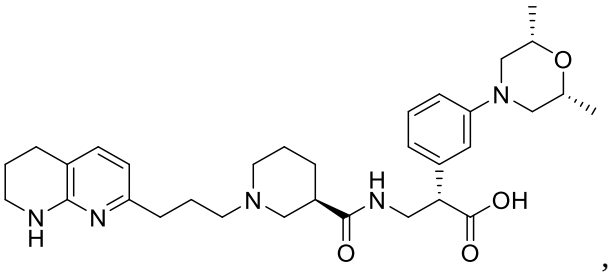
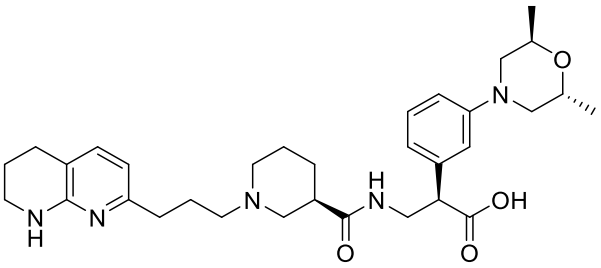
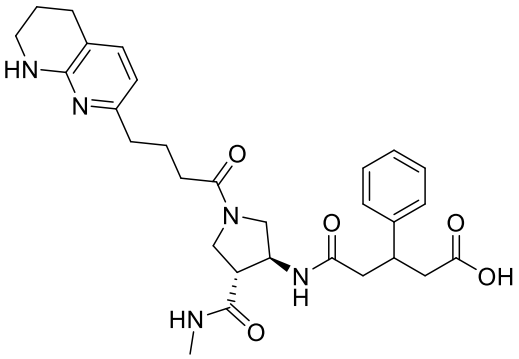
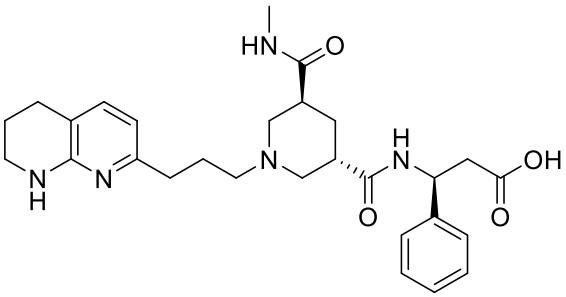
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and

, or pharmaceutically acceptable salts thereof.

81. A pharmaceutical composition comprising pharmaceutically acceptable excipient and a compound or salt of any one of claim 1 to 80.

82. A compound or salt of any one of claims 1 to 80 or a pharmaceutical composition of claim 81, for use in therapy.

83. Use of a compound or salt of any one of claims 1 to 80 or a pharmaceutical composition of claim 81, in the manufacture of a medicament for modulating an alpha V integrin in a subject in need thereof.

84. The use of claim 83, wherein the alpha V integrin is an alpha V beta 1 integrin.

85. The use of claim 83, wherein the alpha V integrin is an alpha V beta 6 integrin.

86. Use of a compound or salt of any one of claims 1 to 80 or a pharmaceutical composition of claim 81, in the manufacture of a medicament for treating a disease or condition in a subject in need thereof.

87. The use of claim 86, wherein the disease or condition is selected from: idiopathic pulmonary fibrosis, systemic lupus erythematosus associated interstitial lung disease, rheumatoid arthritis, diabetic nephropathy, focal segmental glomerulosclerosis, chronic kidney disease, nonalcoholic steatohepatitis, primary biliary cholangitis, primary sclerosing cholangitis, solid tumors, hematological tumors, organ transplant, Alport syndrome, interstitial lung disease, radiation-induced fibrosis, bleomycin-induced fibrosis, asbestos-induced fibrosis, flu-induced fibrosis, coagulation-induced fibrosis, vascular injury-induced fibrosis, aortic stenosis, and cardiac fibrosis.