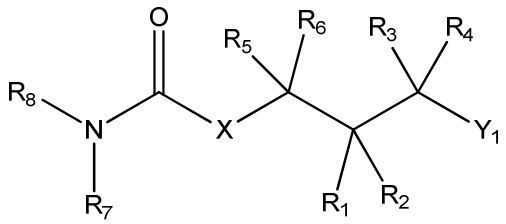
SUMMARY

[003a] In one aspect, the present disclosure refers to a compound of formula I, or a salt, solvate or hydrate thereof,



(I)

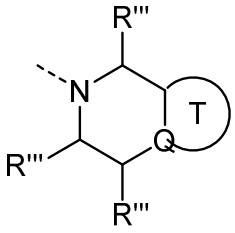
wherein,

R_1, R_3, R_4, R_5 and R_6 are each independently selected from hydrogen and C_{1-3} alkyl;

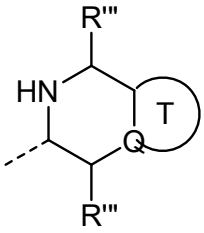
R_2 is selected from hydrogen and OH;

X is O or NR_9, where R_9 is hydrogen or a C_{1-3} alkyl;

Y_1 is a group selected from one of formula A and B,



(A)



(B)

where each R'" is independently selected from H and C_{1-3} alkyl;

Q is C or N;

T is selected from a fused phenyl group and a fused 5- or 6-membered heteroaryl group, wherein each group is optionally substituted with one or more substituents selected from halo and C_{1-3} alkyl; and

R_7 and R_8 are taken together with the intervening nitrogen atom to form a 3-12 membered heterocycloalkyl ring, wherein the 3-12 membered heterocycloalkyl ring is optionally substituted with one or more R_{10}; and/or optionally fused to one or more C_{6-12} aryl, C_{5-12} heteroaryl, C_{3-8} cycloalkyl and 3-12 membered heterocycloalkyl rings, wherein each fused C_{6-12} aryl, C_{5-12} heteroaryl, C_{3-8} cycloalkyl and 3-12 membered heterocycloalkyl ring is optionally substituted with one or more R_{14};

R_{10} is selected from a group of the formula L_1-L_2-R_{11} and L_2-L_1-R_{11}, where L_1 is a linker of the formula $–[CR_{12}R_{13}]_n$-, where n is an integer of from 0 to 3 and R_{12} and R_{13} are in each instance each independently selected from H and C_1 to C_2 alkyl,

where L_2 is absent or a linker that is selected from O, S, SO, SO_2, N(R'), C(O), C(O)O, $[O(CH_2)_r]_s$, $[(CH_2)_rO]_s$, OC(O), CH(OR'), C(O)N(R'), N(R')C(O), N(R')C(O)N(R'), SO_2N(R') and N(R')SO_2, where R' and R" are each independently selected from hydrogen and a C_1 to C_2 alkyl, and where r is 1 or 2 and s is 1 to 4,

R_{11} is independently selected from hydrogen, CN, NO_2, hydroxyl, =O, halogen, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} alkyl, O-C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{6-12} aryl, C_{5-12} heteroaryl, 3-10 membered heterocycloalkyl, $–C(=O)R^d$, $–C(=O)OR^d$, $–C(=O)NR^eR^d$, $–C(O)C(=O)R^d$, $–NR^eR^d$, $–NR^eC(=O)R^d$, $–NR^eC(=O)OR^d$, $–NR^eC(=O)NR^eR^d$, $–NR^eS(=O)_2R^d$, $–NR^eS(=O)_2NR^eR^d$, $–OR^d$, $–SR^d$, $–OC(=O)R^d$, $–OC(=O)NR^eR^d$, $–OC(=O)OR^d$, $–S(=O)_2R^d$, $–S(=O)R^d$, $–OS(=O)R^d$, $–OS(=O)_2R^d$, $–OS(=O)_2OR^d$, $–S(=O)NR^eR^d$, $–OS(=O)_2NR^eR^d$, and $–S(=O)_2NR^eR^d$, wherein, where R_{11} is independently selected from C_{3-6} cycloalkyl, C_{6-12} aryl, C_{5-12} heteroaryl and 3-10 membered heterocycloalkyl, each C_{3-6} cycloalkyl, C_{6-12} aryl, C_{5-12} heteroaryl and 3-10 membered heterocycloalkyl is optionally substituted with one or more R_{14};

each R^a and R^b is independently selected from hydrogen and C_{1-6} alkyl;

each R^d is independently selected from hydrogen, hydroxyl, halogen, CN, C_{1-6} haloalkyl, 3-7 membered heterocycloalkyl, C_{3-6} cycloalkyl, C_{1-6} alkyl, O-C_{1-6} alkyl and C_{6-11} aryl, wherein said C_{1-6} alkyl, C_{6-11} aryl, 3-7 membered heterocycloalkyl and C_{3-6} cycloalkyl are optionally substituted with one or more groups selected from hydroxyl, =O, halogen, CN, COR^a, NR^aR^b, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, C_{6-11} aryl, 3-7 membered heterocycloalkyl, C_{1-6} alkyl and O-C_{1-6} alkyl;

each R^e is independently selected from hydrogen, hydroxyl, halogen, CN, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, C_{1-6} alkyl and O-C_{1-6} alkyl; or

R^e and R^d, when attached to the same atom, together with the atom to which they are attached form a 3-7 membered heterocycloalkyl ring, optionally substituted with one or more substituent selected from hydroxyl, =O, halogen, CN, COR^a, NR^aR^b, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, C_{6-11} aryl, 3-7 membered heterocycloalkyl, C_{1-6} alkyl and O-C_{1-6} alkyl;

and

R^{14} is independently selected from halo, CN, NO_2, hydroxyl, =O, halogen, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} alkyl, O-C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{6-12} aryl, 5-6 membered heteroaryl, 3-7 membered heterocycloalkyl, C_{1-6}alkylC_{6-12}aryl, $–C(=O)R^d$, $–C(=O)OR^d$, $–C(=O)NR^eR^d$, $–C(O)C(=O)R^d$, $–NR^eR^d$, $–NR^eC(=O)R^d$, $–NR^eC(=O)OR^d$, $–NR^eC(=O)NR^eR^d$, $–NR^eS(=O)_2R^d$, $–NR^eS(=O)_2NR^eR^d$, $–OR^d$, $–SR^d$, $–OC(=O)R^d$, $–OC(=O)NR^eR^d$, $–OC(=O)OR^d$,

$-S(=O)_2R^d$, $-S(=O)R^d$, $-OS(=O)R^d$, $-OS(=O)_2R^d$, $-OS(=O)_2OR^d$, $-S(=O)NR^eR^d$, $-OS(=O)_2NR^eR^d$, and $-S(=O)_2NR^eR^d$.

[003b] In another aspect, the present disclosure refers to a pharmaceutical composition which comprises a compound as disclosed herein, or a pharmaceutically acceptable salt, hydrate or solvate thereof, and one or more pharmaceutically acceptable excipients.

[003c] In another aspect, the present disclosure refers to a compound as disclosed herein, or a pharmaceutically acceptable salt, hydrate or solvate thereof, or a pharmaceutical composition as disclosed herein, for use in therapy.

[003d] In yet another aspect, the present disclosure refers to the use of a compound according to any one of claims 1 to 15, or a pharmaceutically acceptable salt, hydrate or solvate thereof, or a pharmaceutical composition according to claim 16 in the manufacture of a medicament for:

(a) treating a proliferative disorder or

(b) treating a cancer.

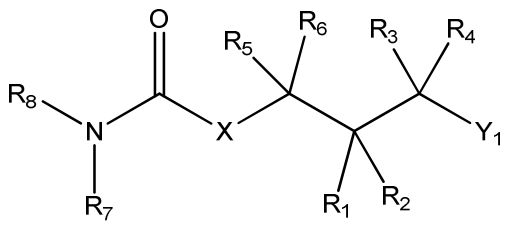
[003e] In yet another aspect, the present disclosure refers to an *in vitro* method of altering gene expression in a cell which comprises contacting a cell with an effective amount of a compound as disclosed herein, or a pharmaceutically acceptable salt, hydrate or solvate thereof, or a pharmaceutical composition as disclosed herein.

[004] In one example, the present disclosure provides a compound of Formula I as defined herein, and/or a salt, hydrate or solvate thereof.

[005] In another example, the present disclosure provides a pharmaceutical composition which comprises a compound of Formula I as defined herein, or a pharmaceutically acceptable salt, hydrate or solvate thereof, and one or more pharmaceutically acceptable excipients.

CLAIMS

1. A compound of formula I, or a salt, solvate or hydrate thereof,



(I)

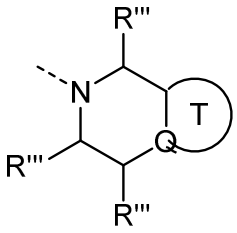
wherein,

R_1, R_3, R_4, R_5 and R_6 are each independently selected from hydrogen and C_{1-3} alkyl;

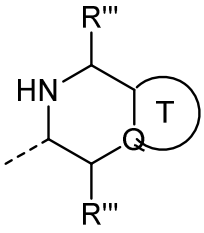
R_2 is selected from hydrogen and OH;

X is O or NR_9, where R_9 is hydrogen or a C_{1-3} alkyl;

Y_1 is a group selected from one of formula A and B,



(A)



(B)

where each R'" is independently selected from H and C_{1-3} alkyl;

Q is C or N;

T is selected from a fused phenyl group and a fused 5- or 6-membered heteroaryl group, wherein each group is optionally substituted with one or more substituents selected from halo and C_{1-3} alkyl; and

R_7 and R_8 are taken together with the intervening nitrogen atom to form a 3-12 membered heterocycloalkyl ring, wherein the 3-12 membered heterocycloalkyl ring is optionally substituted with one or more R_{10}; and/or optionally fused to one or more C_{6-12} aryl, C_{5-12} heteroaryl, C_{3-8} cycloalkyl and 3-12 membered heterocycloalkyl rings, wherein each fused C_{6-12} aryl, C_{5-12} heteroaryl, C_{3-8} cycloalkyl and 3-12 membered heterocycloalkyl ring is optionally substituted with one or more R_{14};

R_{10} is selected from a group of the formula L_1-L_2-R_{11} and L_2-L_1-R_{11}, where L_1 is a linker of the formula $–[CR_{12}R_{13}]_n$-, where n is an integer of from 0 to 3 and R_{12} and R_{13} are in each instance each independently selected from H and C_1 to C_2 alkyl,

where L_2 is absent or a linker that is selected from O, S, SO, SO_2, N(R'), C(O), C(O)O, $[O(CH_2)_r]_s$, $[(CH_2)_rO]_s$, OC(O), CH(OR'), C(O)N(R'), N(R')C(O), N(R')C(O)N(R'), SO_2N(R') and N(R')SO_2, where R' and R" are each independently selected from hydrogen and a C_1 to C_2 alkyl, and where r is 1 or 2 and s is 1 to 4,

R_{11} is independently selected from hydrogen, CN, NO_2, hydroxyl, =O, halogen, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} alkyl, O-C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{6-12} aryl, C_{5-12} heteroaryl, 3-10 membered heterocycloalkyl, $–C(=O)R^d$, $–C(=O)OR^d$, $–C(=O)NR^eR^d$, $–C(O)C(=O)R^d$, $–NR^eR^d$, $–NR^eC(=O)R^d$, $–NR^eC(=O)OR^d$, $–NR^eC(=O)NR^eR^d$, $–NR^eS(=O)_2R^d$, $–NR^eS(=O)_2NR^eR^d$, $–OR^d$, $–SR^d$, $–OC(=O)R^d$, $–OC(=O)NR^eR^d$, $–OC(=O)OR^d$, $–S(=O)_2R^d$, $–S(=O)R^d$, $–OS(=O)R^d$, $–OS(=O)_2R^d$, $–OS(=O)_2OR^d$, $–S(=O)NR^eR^d$, $–OS(=O)_2NR^eR^d$, and $–S(=O)_2NR^eR^d$, wherein, where R_{11} is independently selected from C_{3-6} cycloalkyl, C_{6-12} aryl, C_{5-12} heteroaryl and 3-10 membered heterocycloalkyl, each C_{3-6} cycloalkyl, C_{6-12} aryl, C_{5-12} heteroaryl and 3-10 membered heterocycloalkyl is optionally substituted with one or more R_{14};

each R^a and R^b is independently selected from hydrogen and C_{1-6} alkyl;

each R^d is independently selected from hydrogen, hydroxyl, halogen, CN, C_{1-6} haloalkyl, 3-7 membered heterocycloalkyl, C_{3-6} cycloalkyl, C_{1-6} alkyl, O-C_{1-6} alkyl and C_{6-11} aryl, wherein said C_{1-6} alkyl, C_{6-11} aryl, 3-7 membered heterocycloalkyl and C_{3-6} cycloalkyl are optionally substituted with one or more groups selected from hydroxyl, =O, halogen, CN, COR^a, NR^aR^b, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, C_{6-11} aryl, 3-7 membered heterocycloalkyl, C_{1-6} alkyl and O-C_{1-6} alkyl;

each R^e is independently selected from hydrogen, hydroxyl, halogen, CN, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, C_{1-6} alkyl and O-C_{1-6} alkyl; or

R^e and R^d, when attached to the same atom, together with the atom to which they are attached form a 3-7 membered heterocycloalkyl ring, optionally substituted with one or more substituent selected from hydroxyl, =O, halogen, CN, COR^a, NR^aR^b, C_{1-6} haloalkyl, C_{3-6} cycloalkyl, C_{6-11} aryl, 3-7 membered heterocycloalkyl, C_{1-6} alkyl and O-C_{1-6} alkyl;

and

R^{14} is independently selected from halo, CN, NO_2, hydroxyl, =O, halogen, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} alkyl, O-C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{6-12} aryl, 5-6 membered heteroaryl, 3-7 membered heterocycloalkyl, C_{1-6}alkylC_{6-12}aryl, $–C(=O)R^d$, $–C(=O)OR^d$, $–C(=O)NR^eR^d$, $–C(O)C(=O)R^d$, $–NR^eR^d$, $–NR^eC(=O)R^d$, $–NR^eC(=O)OR^d$, $–NR^eC(=O)NR^eR^d$, $–NR^eS(=O)_2R^d$, $–NR^eS(=O)_2NR^eR^d$, $–OR^d$, $–SR^d$, $–OC(=O)R^d$, $–OC(=O)NR^eR^d$, $–OC(=O)OR^d$, $–S(=O)_2R^d$, $–S(=O)R^d$, $–OS(=O)R^d$, $–OS(=O)_2R^d$, $–OS(=O)_2OR^d$, $–S(=O)NR^eR^d$, $–OS(=O)_2NR^eR^d$, and $–S(=O)_2NR^eR^d$.

2. A compound according to claim 1, or a salt, solvate or hydrate thereof, wherein:

(a) X is NH or O;

(b) R_1, R_3, R_4, R_5 and R_6 are each hydrogen;

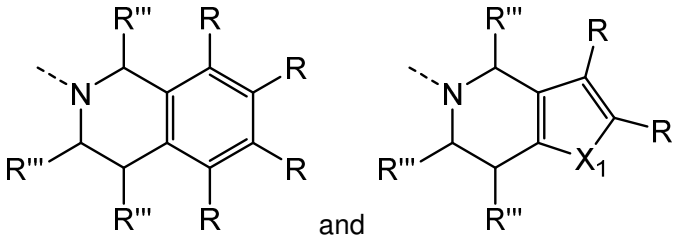
(c) Y_1 is a group of the formula A; and/or

(d) Q is C.

3. A compound according to claim 1 or claim 2, or a salt, solvate or hydrate thereof, wherein T is a fused phenyl which is optionally substituted with one or more substituents selected from halo and C_1 to C_3 alkyl.

4. A compound according to claim 1 or claim 2, or a salt, solvate or hydrate thereof, wherein T is a fused 5- or 6-membered heteroaryl group optionally substituted with one or more substituents selected from halo and C_1 to C_3 alkyl.

5. A compound according to claim 1 or claim 2, or a salt, solvate or hydrate thereof, wherein Y_1 is selected from



wherein each R and R''' is selected from H and C_1 to C_3 alkyl, and X_1 is S.

6. A compound according to any preceding claim, or a salt, solvate or hydrate thereof, wherein the 3-12 membered heterocycloalkyl ring formed by R_7 and R_8 taken together with the intervening nitrogen atom is a 4-7 membered heterocycloalkyl ring, and optionally wherein the intervening nitrogen atom is the sole heteroatom in the 4-7 membered heterocycloalkyl ring.

7. A compound according to claim 6, or a salt, solvate or hydrate thereof, wherein either:

(a) the 4-7 membered heterocycloalkyl ring is selected from a pyrrolidinyl, piperidinyl and azepanyl ring; or

(b) the 4-7 membered heterocycloalkyl ring comprises a second heteroatom, and optionally wherein the second heteroatom is selected from O, S and N, and further optionally wherein the 4-7 membered heterocycloalkyl ring is selected from a piperizinyl, morpholinyl and diazepanyl ring.

8. A compound according to any preceding claim, or a salt, solvate or hydrate thereof, wherein the 3-12 membered heterocycloalkyl ring formed by R_7 and R_8 taken together with the intervening nitrogen atom is a 4-7 membered heterocycloalkyl ring, which is either:

(a) unsubstituted; or

(b) substituted with one or more R_{10}, and optionally wherein (i) R_{11} is independently selected from hydroxyl, C_{1-6} alkyl, C_{6-12} aryl, C_{5-12} heteroaryl and $–C(=O)R^d$, wherein, where R_{11} is selected from C_{6-12} aryl and/or C_{5-12} heteroaryl, the C_{6-12} aryl and/or C_{5-12} heteroaryl is optionally substituted with R_{14}, and further optionally wherein (ii) R_{11} is independently selected from C_{6-12} aryl and/or C_{5-12} heteroaryl that is optionally substituted with R_{14}, and optionally wherein R_{11} is independently selected from phenyl that is optionally substituted with R_{14}.

9. A compound according to any preceding claim, or a salt, solvate or hydrate thereof, wherein L_1 is a linker of the formula $–[CR_{12}R_{13}]_n-$, where n is an integer of from 0 to 3, and R_{12} and R_{13} are in each instance each independently selected from H or C_1 to C_2 alkyl, and where L_2 is absent or a linker that is selected from O.

10. A compound according to any preceding claim, or a salt, solvate or hydrate thereof, wherein the 3-12 membered heterocycloalkyl ring formed by R_7 and R_8 taken together with the intervening nitrogen atom is fused to one or more C_{6-12} aryl, C_{5-12} heteroaryl, C_{3-8} cycloalkyl and 3-12 membered heterocycloalkyl rings, wherein each fused C_{6-12} aryl, C_{5-12} heteroaryl, C_{3-8} cycloalkyl and 3-12 membered heterocycloalkyl ring is optionally substituted with R_{14}.

11. A compound according to claim 10, or a salt, solvate or hydrate thereof, wherein R_{14} is absent or selected from C_{1-3} alkyl, halo or hydroxyl.

12. A compound according to claim 10 or 11, or a salt, solvate or hydrate thereof, wherein the 3-12 membered heterocycloalkyl ring is fused to one or more C_{6-12} aryl groups and/or C_{5-12} heteroaryl groups, said C_{6-12} aryl groups and/or C_{5-12} heteroaryl groups being optionally substituted with R_{14}, and optionally wherein the 3-12 membered heterocycloalkyl ring is fused to a phenyl group that is optionally substituted with R_{14}.

13. A compound according to any one of claims 10 to 12, or a salt, solvate or hydrate thereof, wherein the 3-12 membered heterocycloalkyl ring is selected from a pyrrolidinyl, piperidinyl and azepanyl ring.

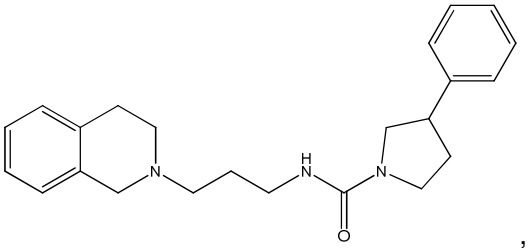
14. A compound according to any preceding claim, or a salt, solvate or hydrate thereof, wherein R_7 and R_8 are taken together with the intervening nitrogen atom to form a 4-7 membered heterocycloalkyl ring, wherein the 4 to 7 membered heterocycloalkyl ring is

(i) unsubstituted, or either

(ii) substituted with at least one R_{10}, where R_{10} is L_1-L_2-R_{11} or L_2-L_1-R_{11}, where L_1 is a linker of the formula $–[CR_{12}R_{13}]_n$-, where n is an integer of from 0 to 3 and R_{12} and R_{13} are in each instance each independently selected from H or C_1 to C_2 alkyl, and where L_2 is absent or a linker that is selected from O, C(O) or N(R'), where R' is H or C_1 to C_2 alkyl, and R_{11} is $-S(=O)_2R_d$, C_{6-12} aryl (e.g. phenyl), 3 – 10 membered heterocycloalkyl or C_{5-12} heteroaryl, wherein the C_{6-12} aryl, 3 – 10 membered heterocycloalkyl and/or C_{5-12} heteroaryl is optionally substituted with one or more R_{14}; and/or

(iii) fused to at least one C_{6-12} aryl (e.g. phenyl), or C_{5-12} heteroaryl; wherein the C_{6-12} aryl and/or C_{5-12} heteroaryl is optionally substituted with one or more R_{14}.

15. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt, hydrate or solvate thereof, wherein the compound is not any of the following compounds: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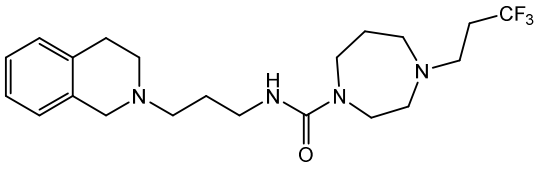
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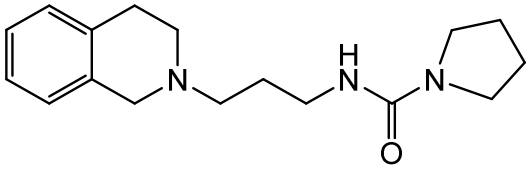
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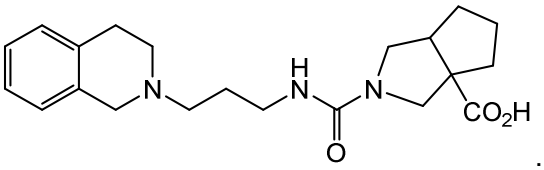
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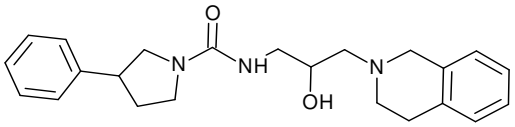
16. A compound, or a salt, solvate or hydrate thereof, selected from: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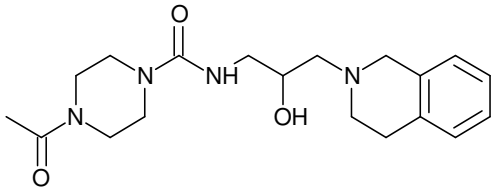
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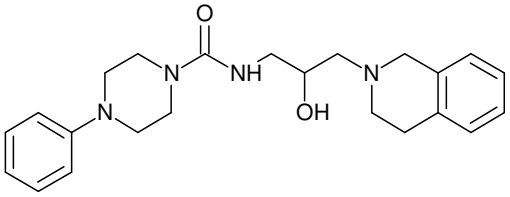
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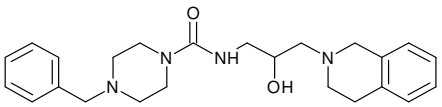
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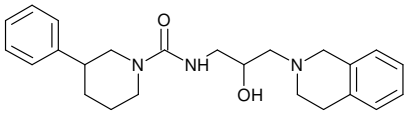
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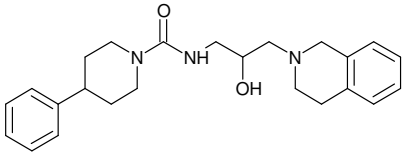
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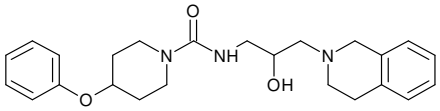
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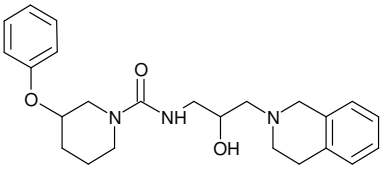
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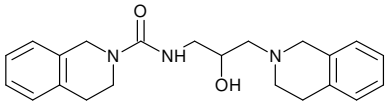
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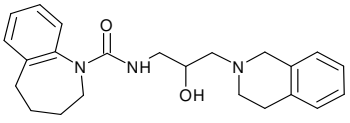
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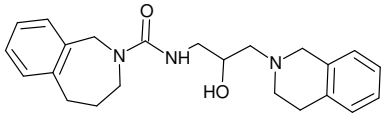
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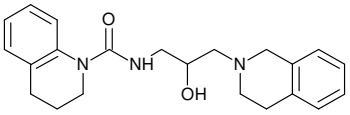
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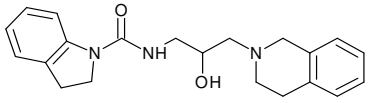
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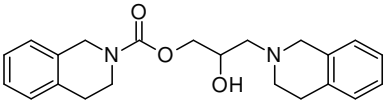
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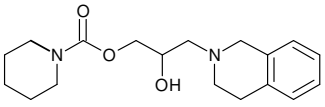
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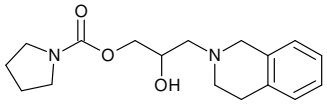
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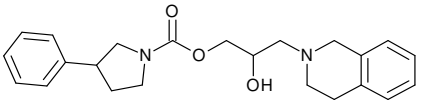
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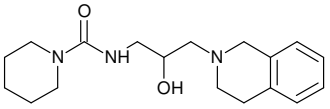
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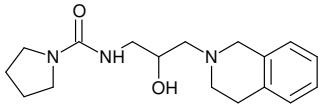
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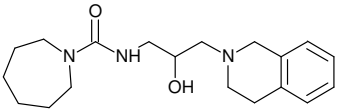
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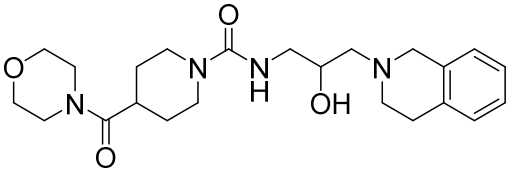
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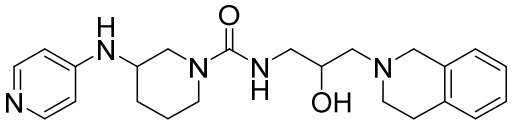
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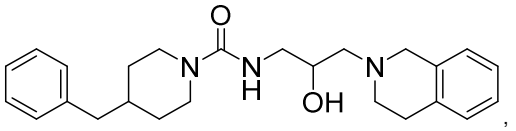
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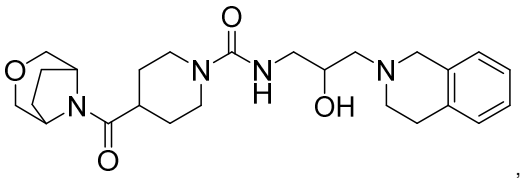
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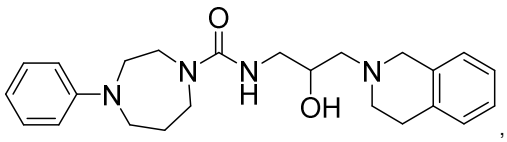
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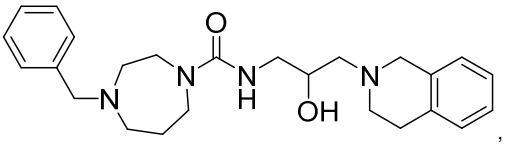
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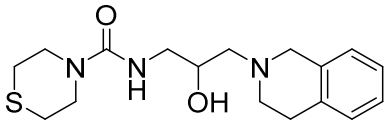
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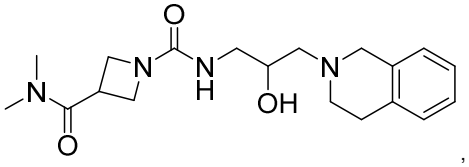
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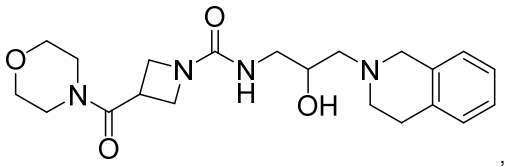
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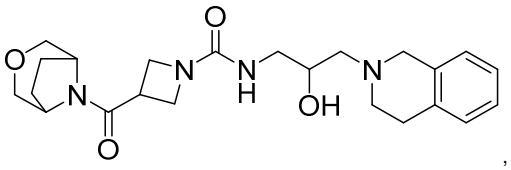
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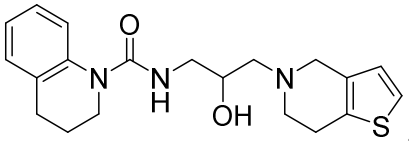
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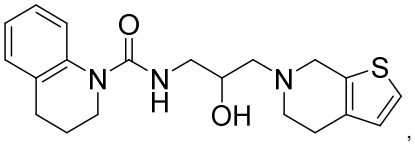
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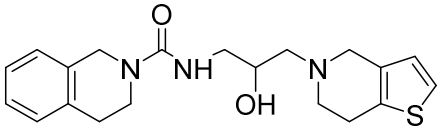
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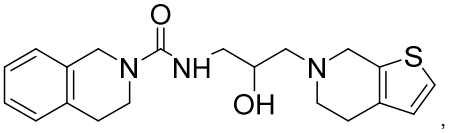
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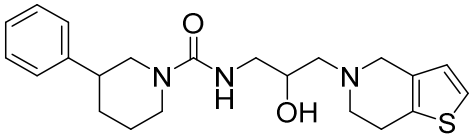
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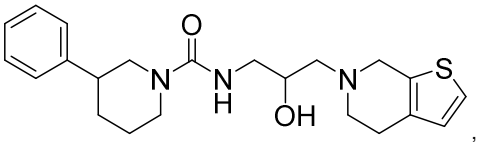
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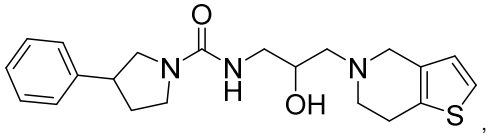
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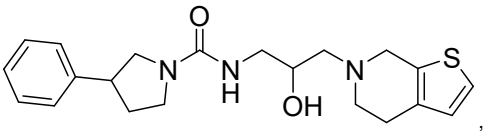
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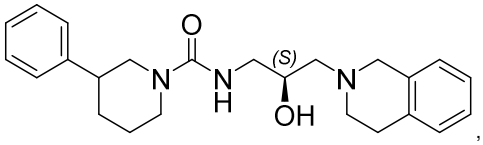
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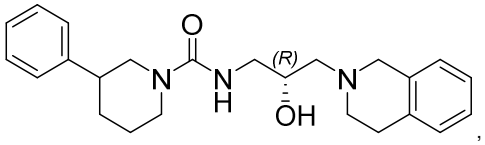
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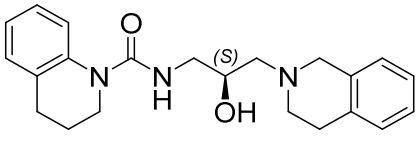
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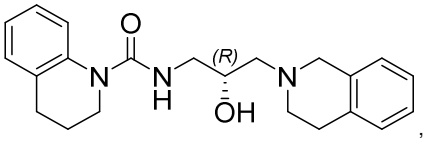
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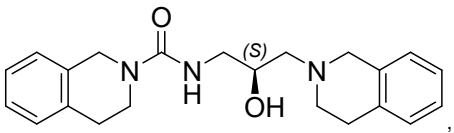
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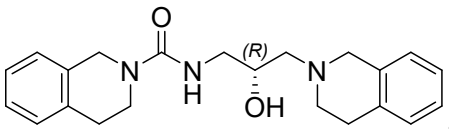
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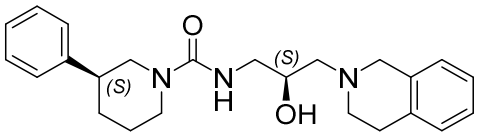
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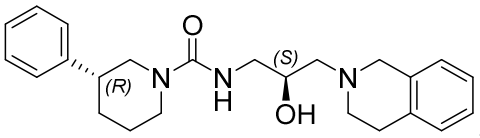
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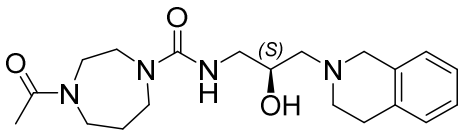
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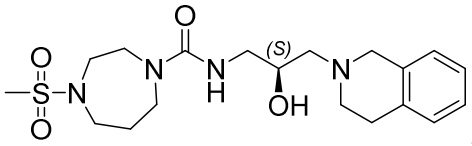
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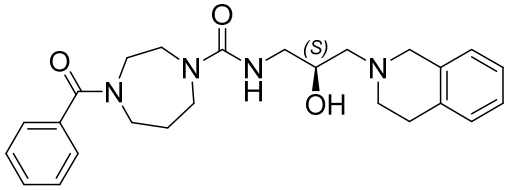
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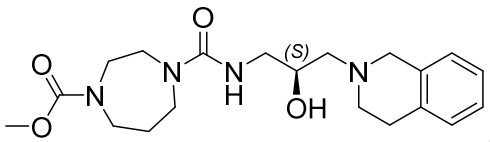
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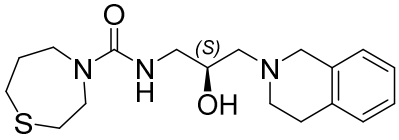
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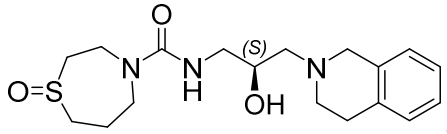
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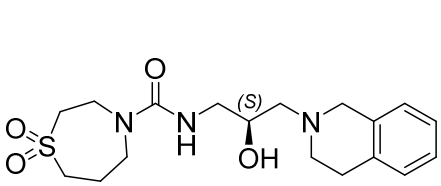
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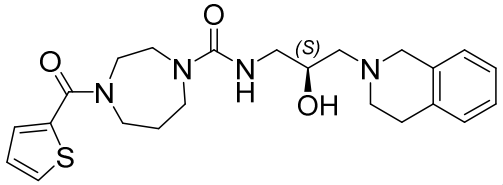
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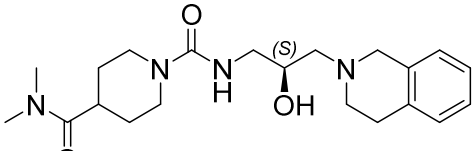
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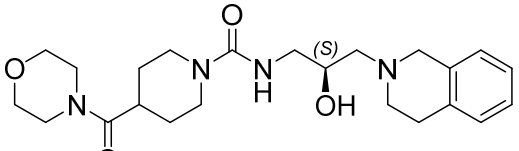
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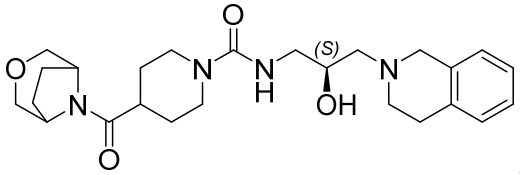
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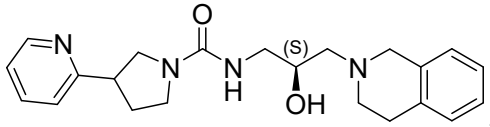
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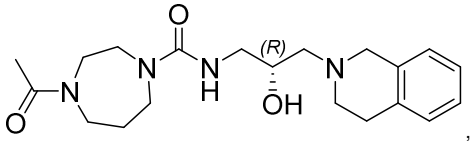
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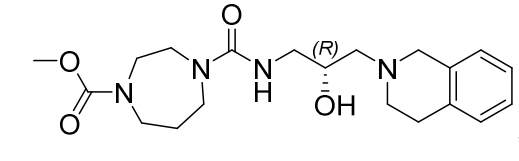
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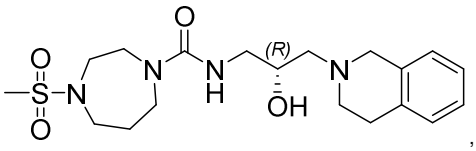

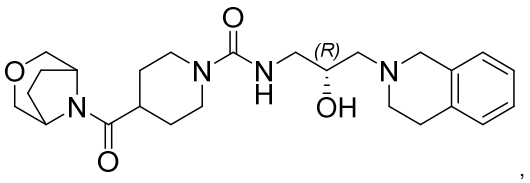

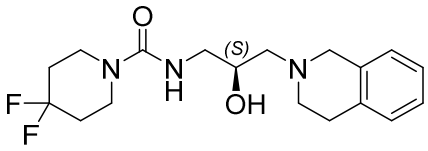

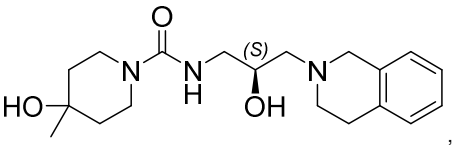

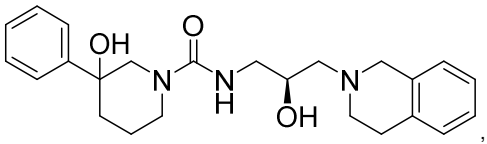

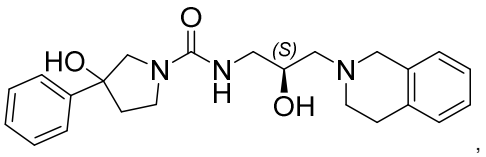

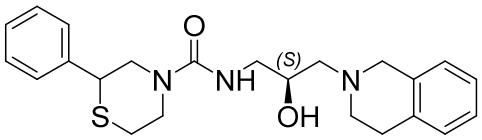

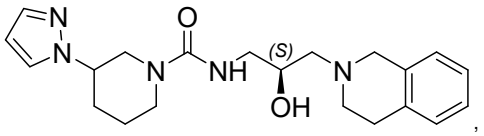

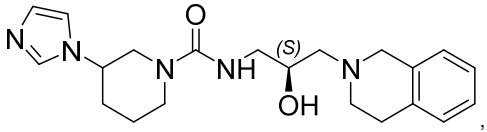

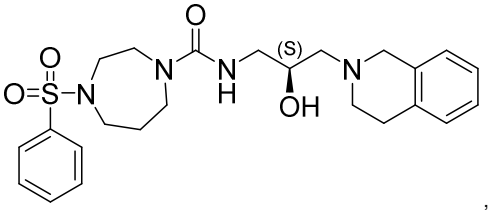

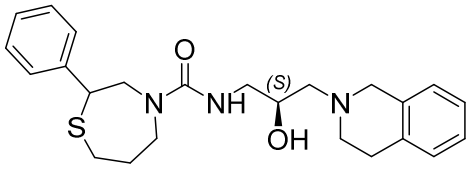

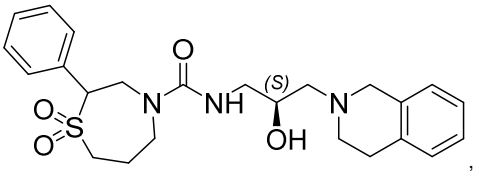

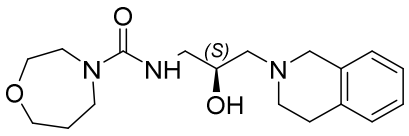

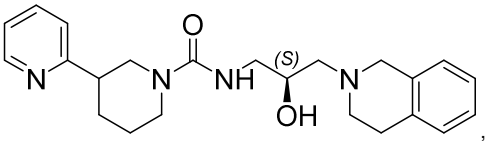

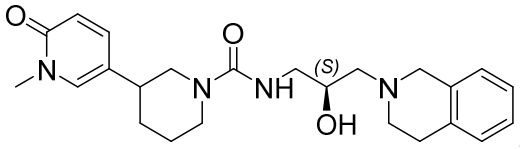

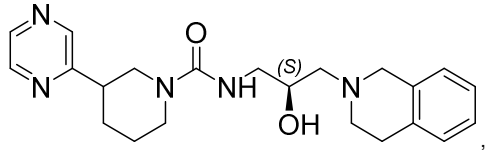

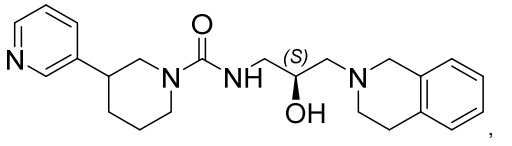

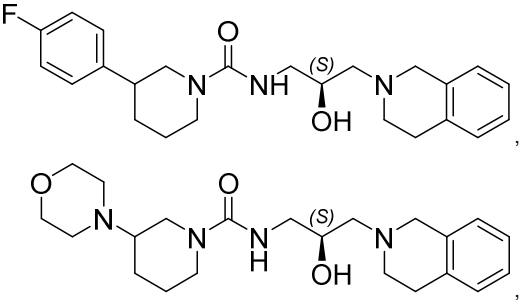

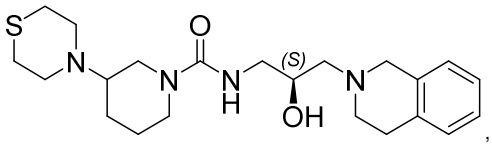
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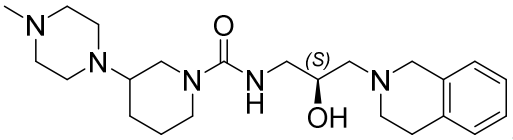
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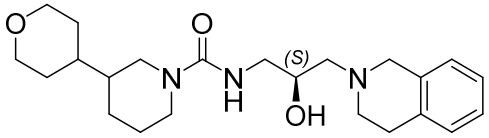
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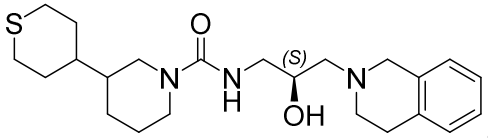
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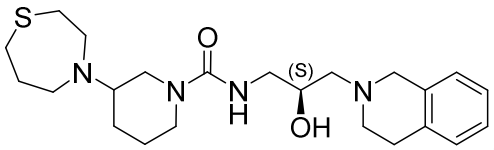
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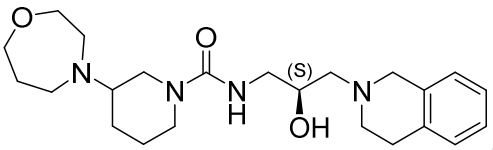
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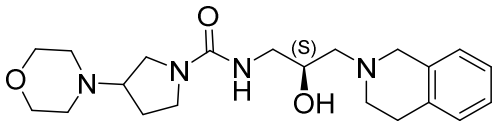
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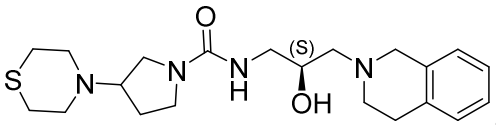
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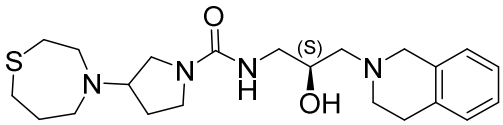
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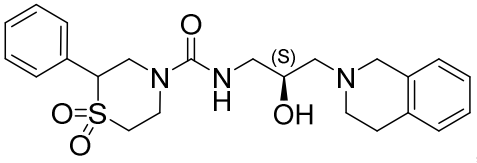
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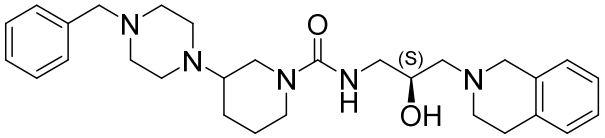
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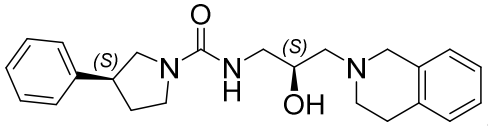
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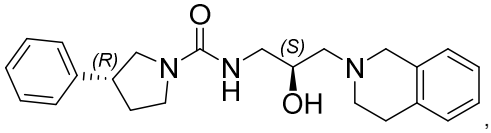
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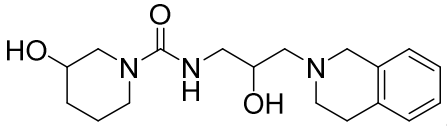
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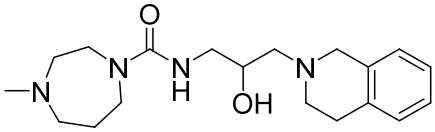
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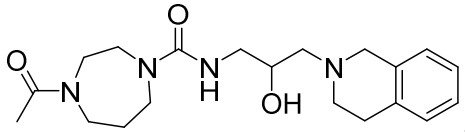
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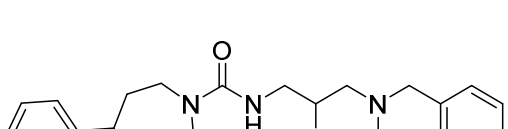
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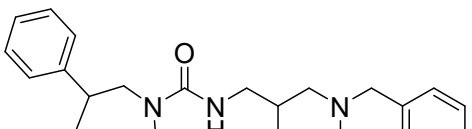
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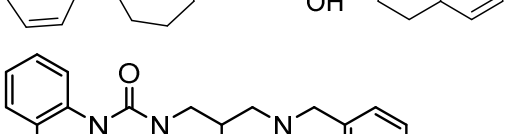
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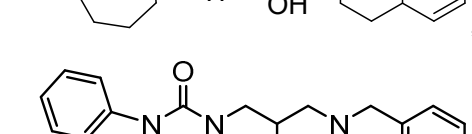
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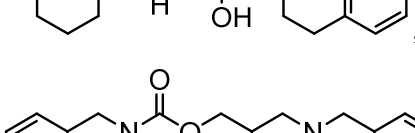
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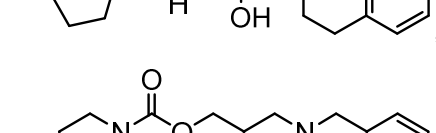
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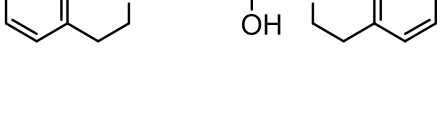
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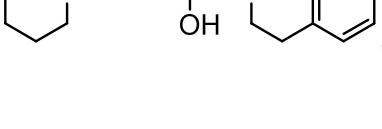
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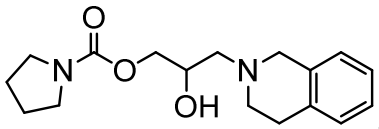
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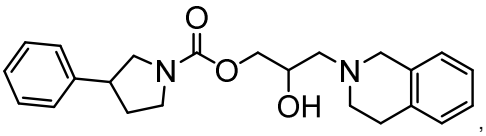
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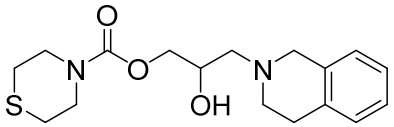
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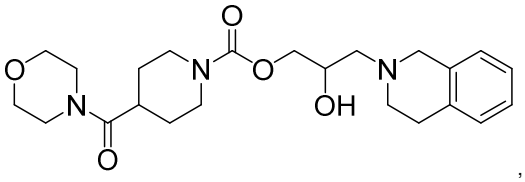
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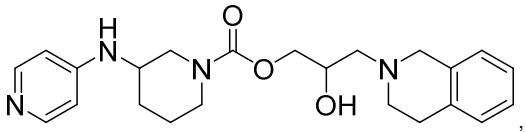
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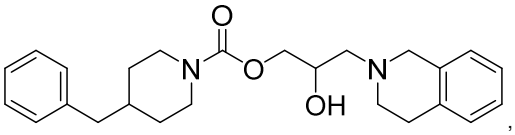
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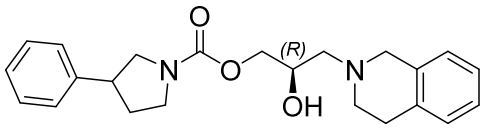
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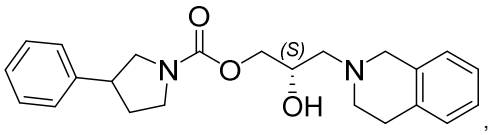
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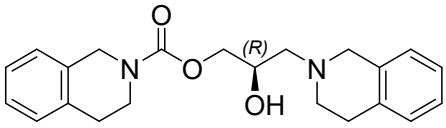
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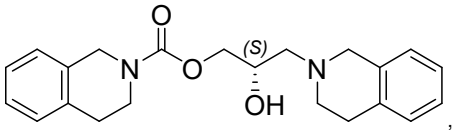
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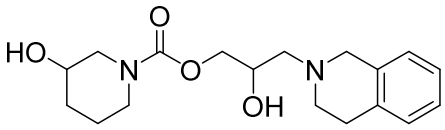
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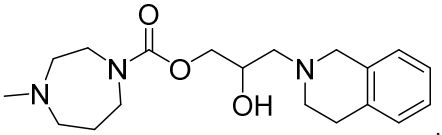
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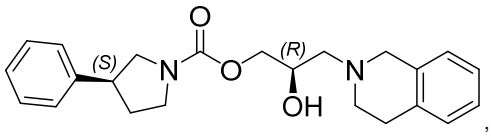
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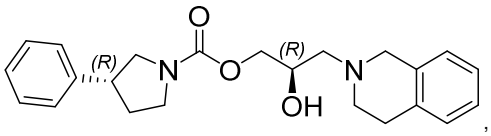
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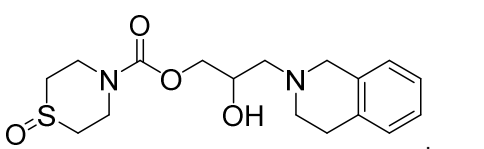
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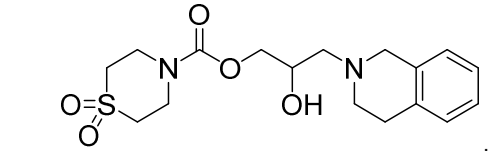
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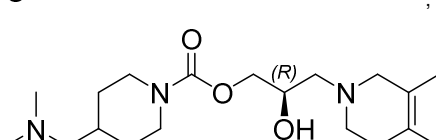
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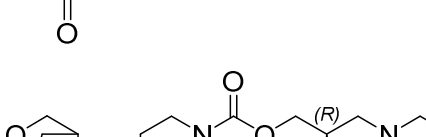
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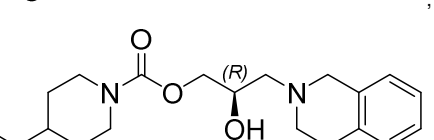
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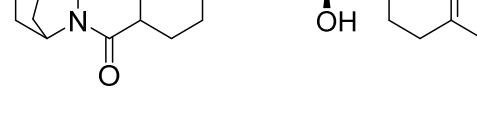
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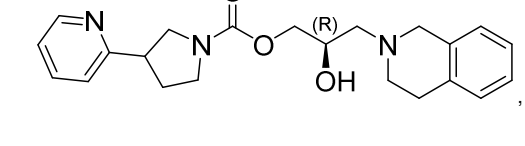
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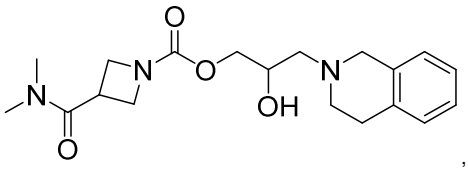
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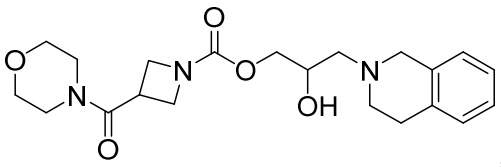
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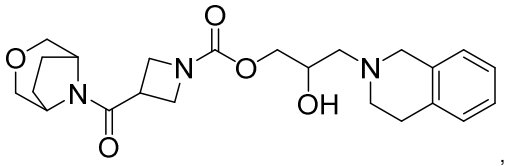
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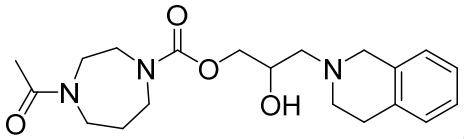
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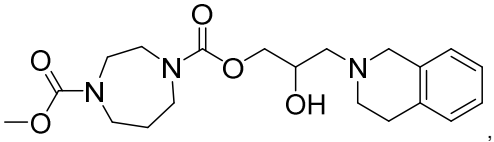
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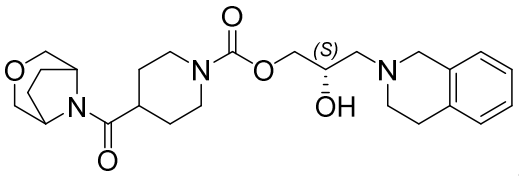
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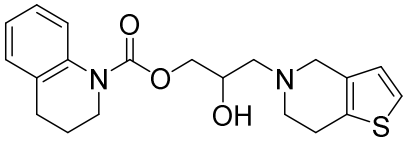
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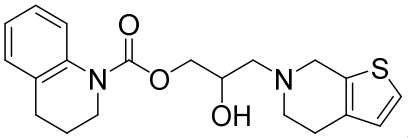
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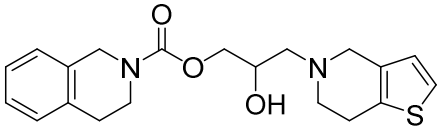
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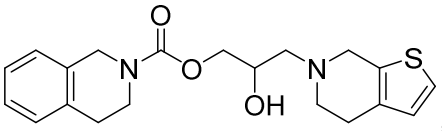
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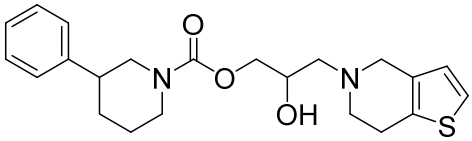
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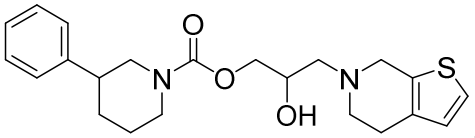
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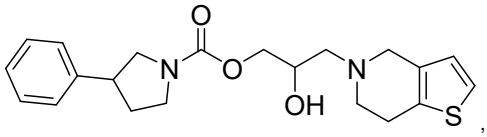
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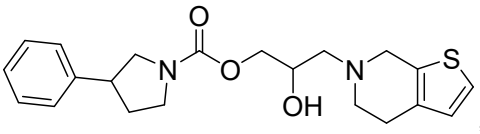
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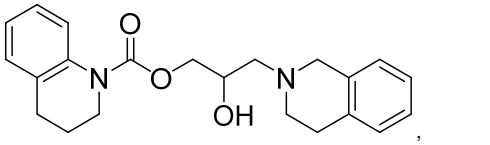
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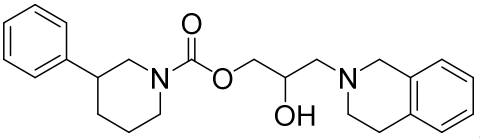
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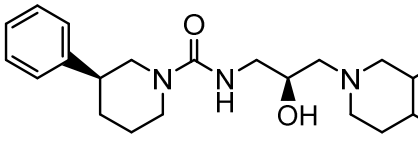
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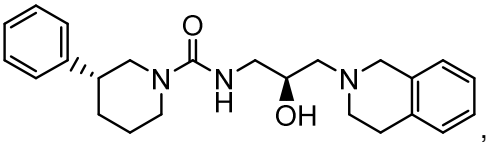
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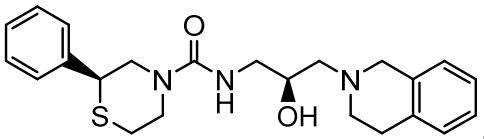
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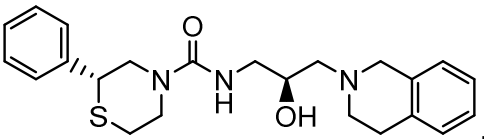
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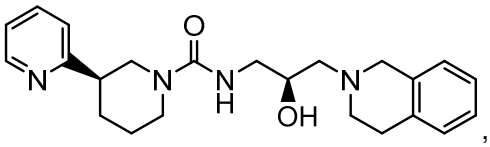
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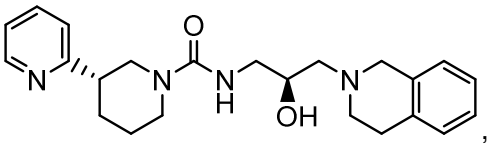
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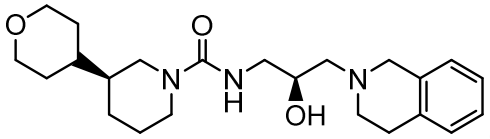
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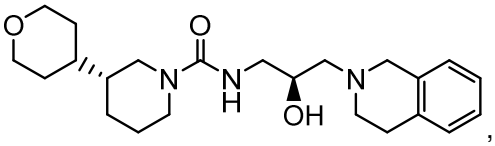
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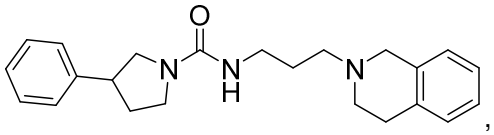
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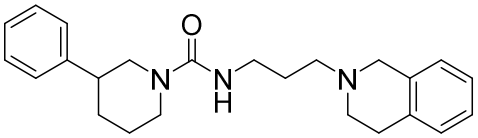
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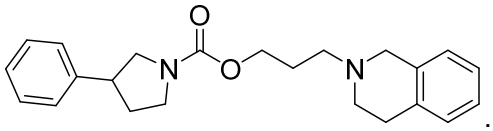
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17. A pharmaceutical composition which comprises a compound according to any one of claims 1 to 16, or a pharmaceutically acceptable salt, hydrate or solvate thereof, and one or more pharmaceutically acceptable excipients.

18. A compound according to any one of claims 1 to 16, or a pharmaceutically acceptable salt, hydrate or solvate thereof, or a pharmaceutical composition according to claim 17, for use in therapy.

19. Use of a compound according to any one of claims 1 to 16, or a pharmaceutically acceptable salt, hydrate or solvate thereof, or a pharmaceutical composition according to claim 17 in the manufacture of a medicament for (a) treating a proliferative disorder or (b) treating a cancer.

20. An *in vitro* method of altering gene expression in a cell which comprises contacting a cell with an effective amount of a compound according to any one of claims 1 to 16, or a pharmaceutically acceptable salt, hydrate or solvate thereof, or a pharmaceutical composition according to claim 17.