

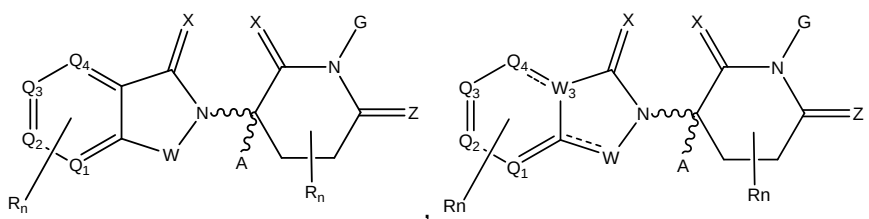
REIVINDICACIONES

1. Un compuesto heterobifuncional que tiene la estructura química:

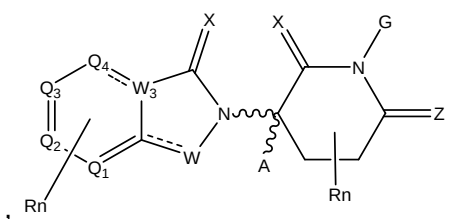
PTM—L—CLM,

o una sal o solvato farmacéuticamente aceptable de este,
en donde:

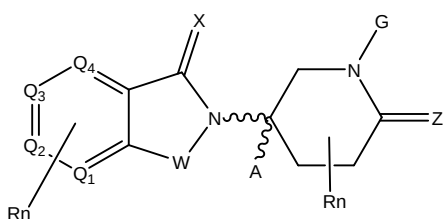
(a) la CLM es un resto de unión a ubiquitina ligasa E3 de micromolécula que se une a una ubiquitina ligasa de cereblon E3 y está representado por la estructura química:



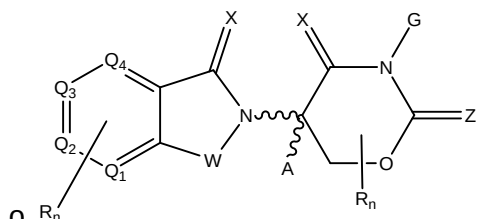
(a1)



(a2)



(a3)



(a4)

en donde:

W es CH₂, C=O, SO₂ o NH;

cada X se selecciona independientemente de ausente, O y S;

Z está ausente, O o S;

G es H o alquilo lineal o ramificado no sustituido o sustituido;

cada Q₁, Q₂, Q₃ y Q₄ es independientemente N, CH o CR;

A es H o alquilo lineal o ramificado no sustituido o sustituido;

n es un número entero de 1 a 10 (por ejemplo, 1-4, 1, 2, 3, 4, 5, 6, 7, 8, 9 o 10);

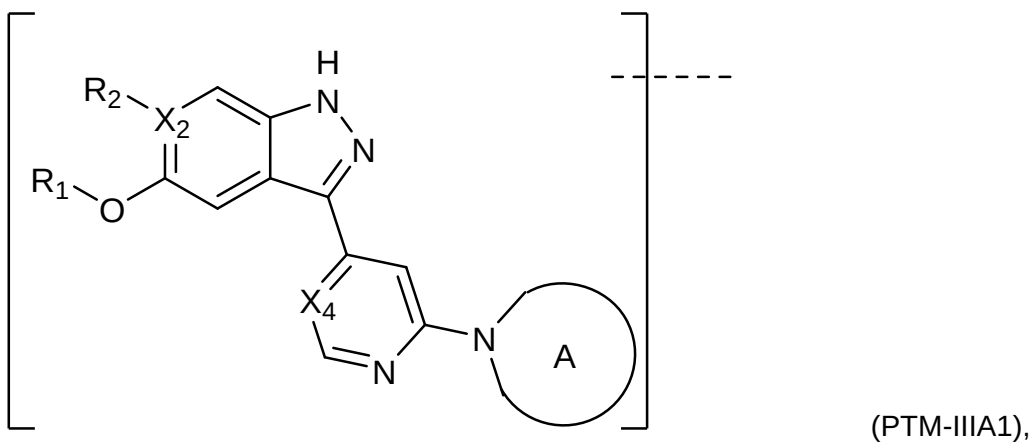
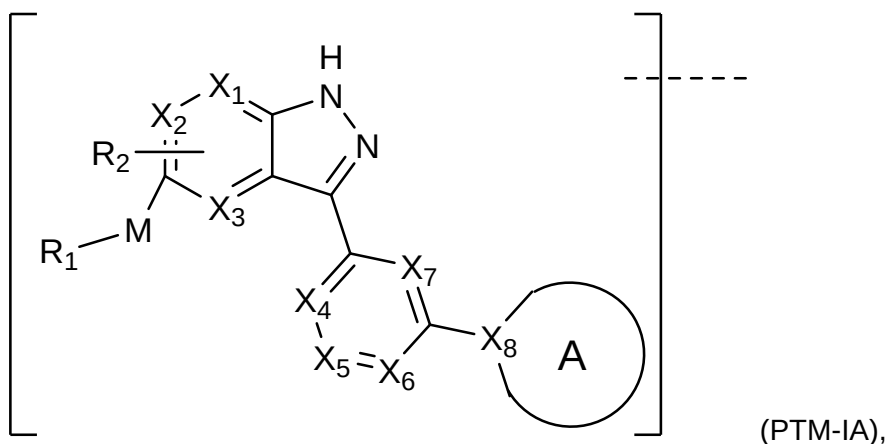
R es un enlace, H, O, -CONR'R'', -C(=O)R', -OR', -NR'R'', alquilo lineal o ramificado no sustituido o sustituido, grupo alcoxilo opcionalmente sustituido, -Cl, -F, -Br, -CF₃ o -CN, en donde un R está unido covalentemente al L; y

R' y R'' se seleccionan independientemente de un enlace, H y alquilo opcionalmente sustituido;

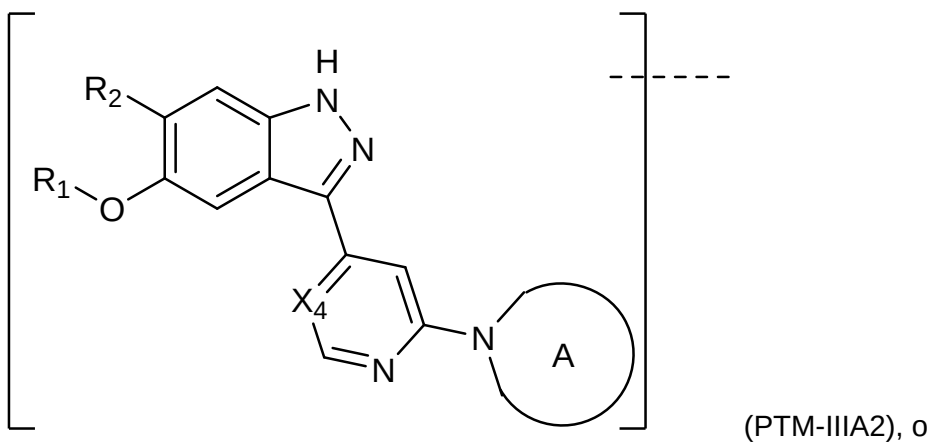
— representa un enlace simple o un enlace doble; y

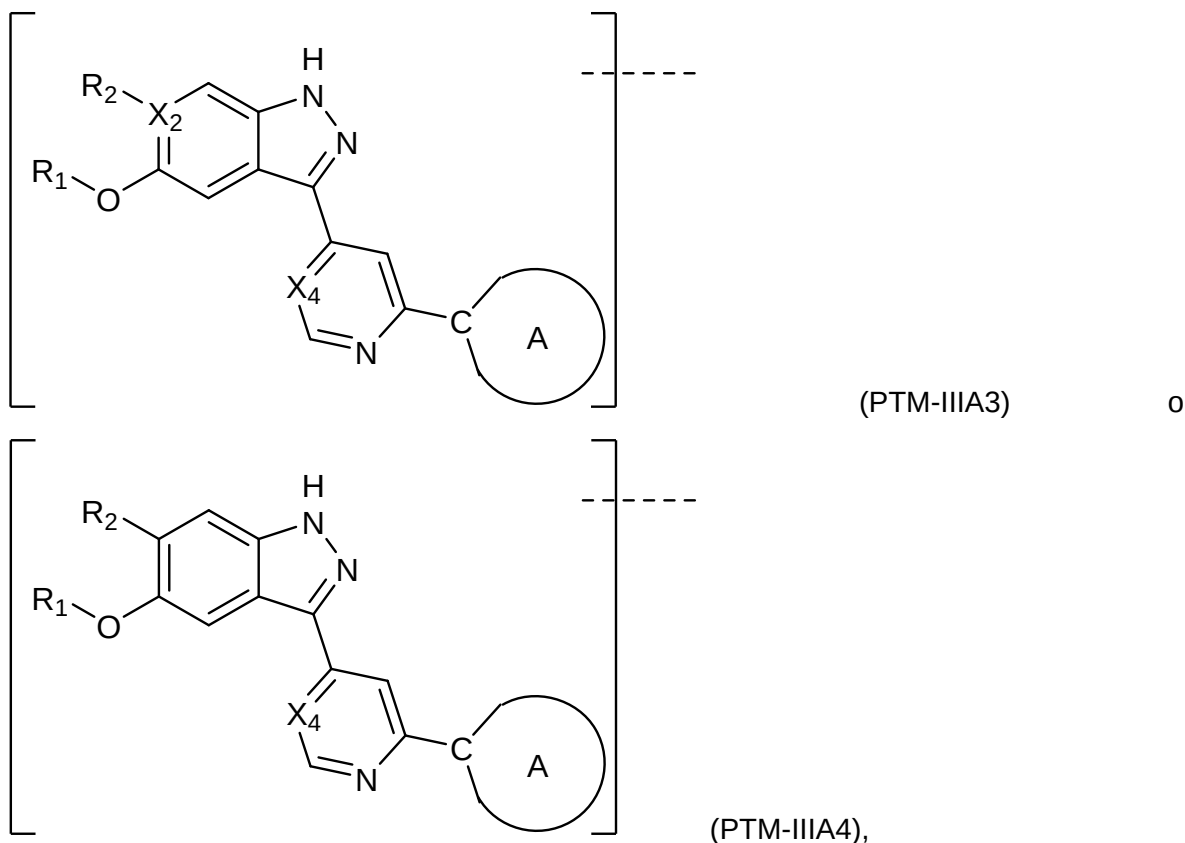
~ representa un enlace que puede ser estereoespecífico ((R) o (S)) o no estereoespecífico;

(b) la PTM es un resto de direccionamiento a cinasa 2 repetida rica en leucina (LRRK2) de micromolécula que se une a LRRK2 o una forma mutante de este representado por la estructura química:

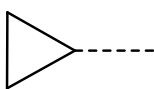


o





en donde:

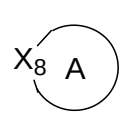
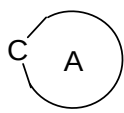
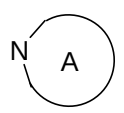
R_1 es un isopropilo, terc-butilo,  o , en donde  es el punto de unión al átomo de oxígeno de la PTM;

R_2 es hidrógeno, F, Cl, OH, alquilo C1-C3 o fluoroalquilo C1-C3;

X_6 y X_7 son cada uno independientemente CH o N;

X_1 , X_2 , X_3 , X_4 y X_5 son cada uno independientemente un N o CH que está opcionalmente sustituido con R_2 cuando CH;

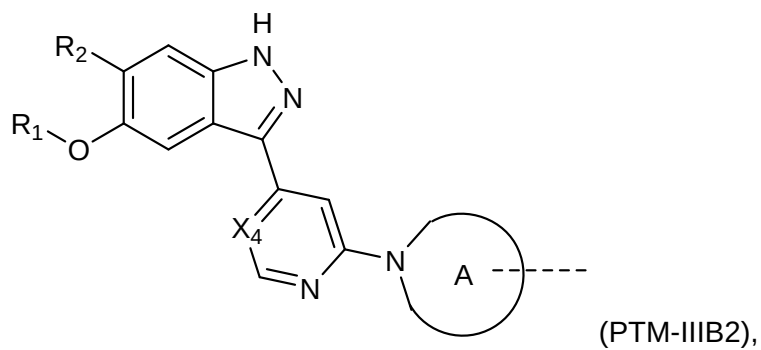
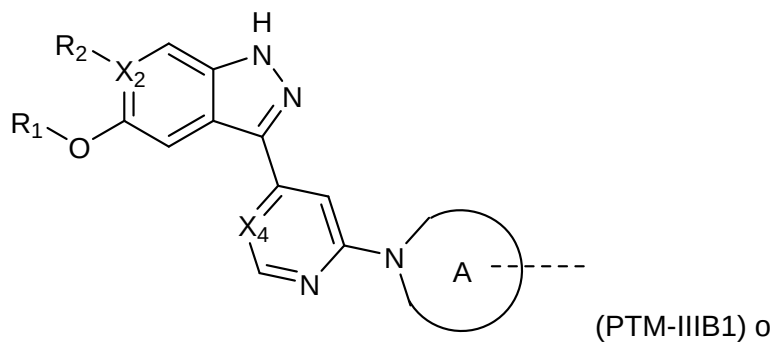
X_8 es CH o N;

,  o  es un cicloalquilo, heterocicloalquilo, bicicloalquilo, biheterocicloalquilo, espirocicloalquilo o espiroheterocicloalquilo de 3-10 miembros opcionalmente sustituido que contiene 1-4 (por ejemplo, 1, 2, 3 o 4) heteroátomos que se seleccionan de N, O y S (por ejemplo, opcionalmente sustituido con una o más (por ejemplo, 1, 2, 3 o 4) sustituciones; y

 del PTM indica el punto de unión con la L; y

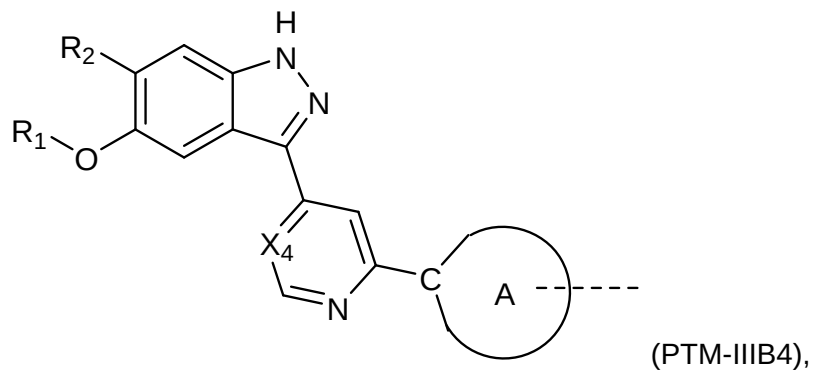
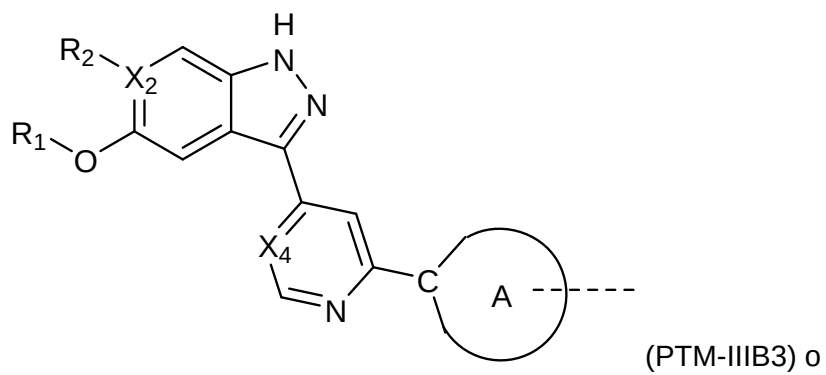
(c) la L es un grupo enlazador químico que acopla covalentemente la CLM a la PTM.

2. El compuesto de la reivindicación 1, en donde la PTM está representada por:



en  donde el PTM indica el punto de unión con la L.

3. El compuesto de la reivindicación 1, en donde la PTM está representada por:



en --- donde el PTM indica el punto de unión con la L.

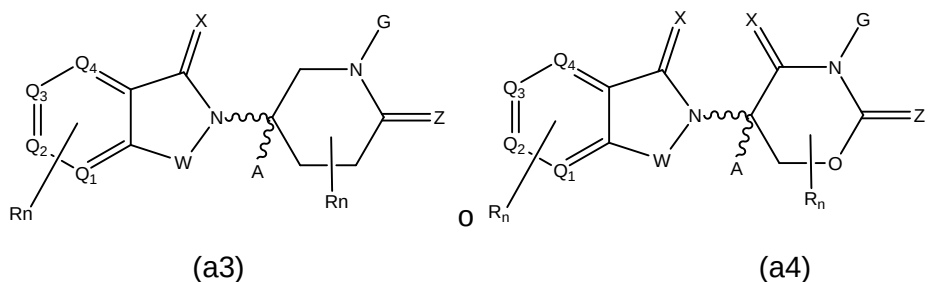
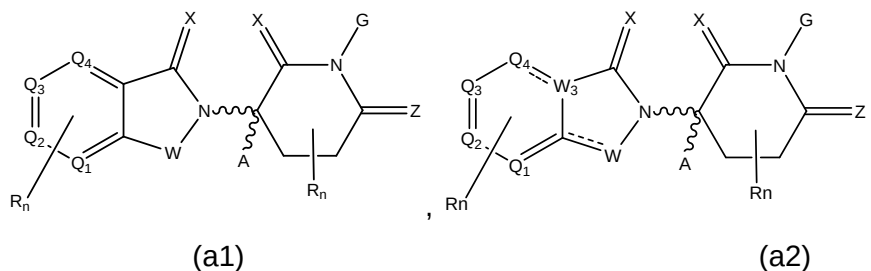
4. Un compuesto heterobifuncional que tiene la estructura química:

PTM—L—CLM,

o una sal o solvato farmacéuticamente aceptable de este,

en donde:

(a) la CLM es un resto de unión a ubiquitina ligasa E3 de micromolécula que se une a una ubiquitina ligasa de cereblon E3 y está representado por la estructura química:



en donde:

W es CH_2 , $\text{C}=\text{O}$, SO_2 o NH ;

cada X se selecciona independientemente de ausente, O y S;

Z está ausente, O o S;

G es H o alquilo lineal o ramificado no sustituido o sustituido;

cada Q_1 , Q_2 , Q_3 y Q_4 es independientemente N, CH o CR;

A es H o alquilo lineal o ramificado no sustituido o sustituido;

n es un número entero de 1 a 10 (por ejemplo, 1-4, 1, 2, 3, 4, 5, 6, 7, 8, 9 o 10);

R es un enlace, H, O, $-\text{CONR}'\text{R}''$, $-\text{C}(=\text{O})\text{R}'$, $-\text{OR}'$, $-\text{NR}'\text{R}''$, alquilo lineal o ramificado no sustituido o sustituido, grupo alcoxilo opcionalmente sustituido, $-\text{Cl}$, $-\text{F}$, $-\text{Br}$, $-\text{CF}_3$ o $-\text{CN}$, en donde un R está unido covalentemente al L; y

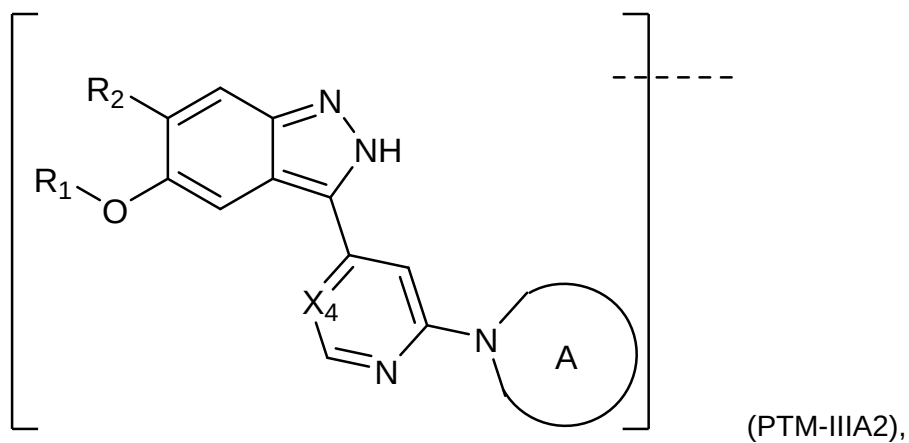
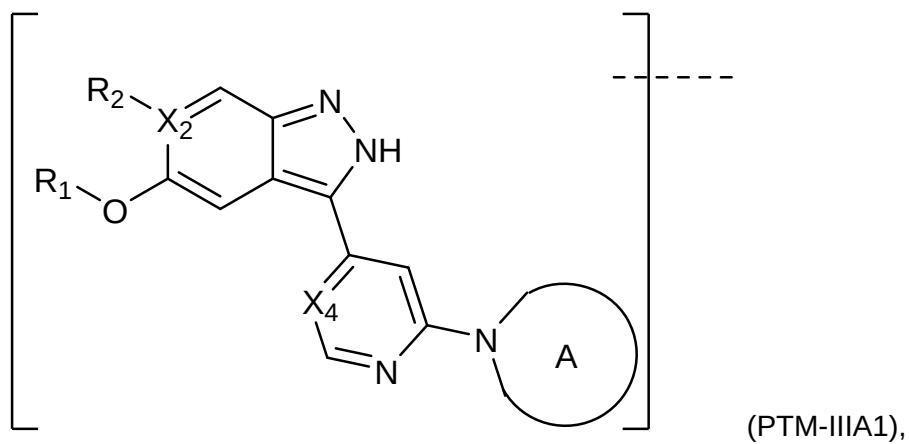
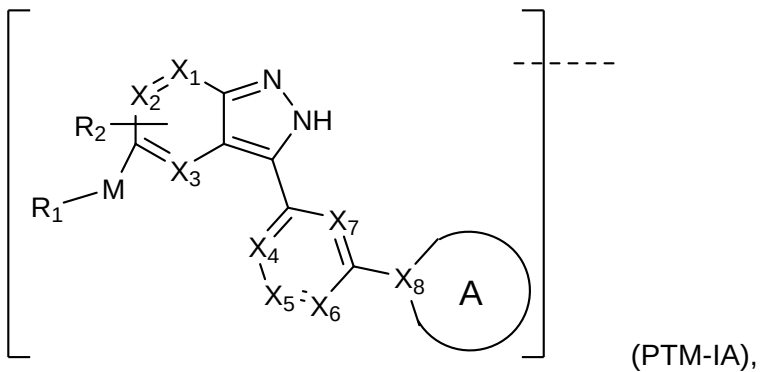
R' y R'' se seleccionan independientemente de un enlace, H y alquilo opcionalmente sustituido;

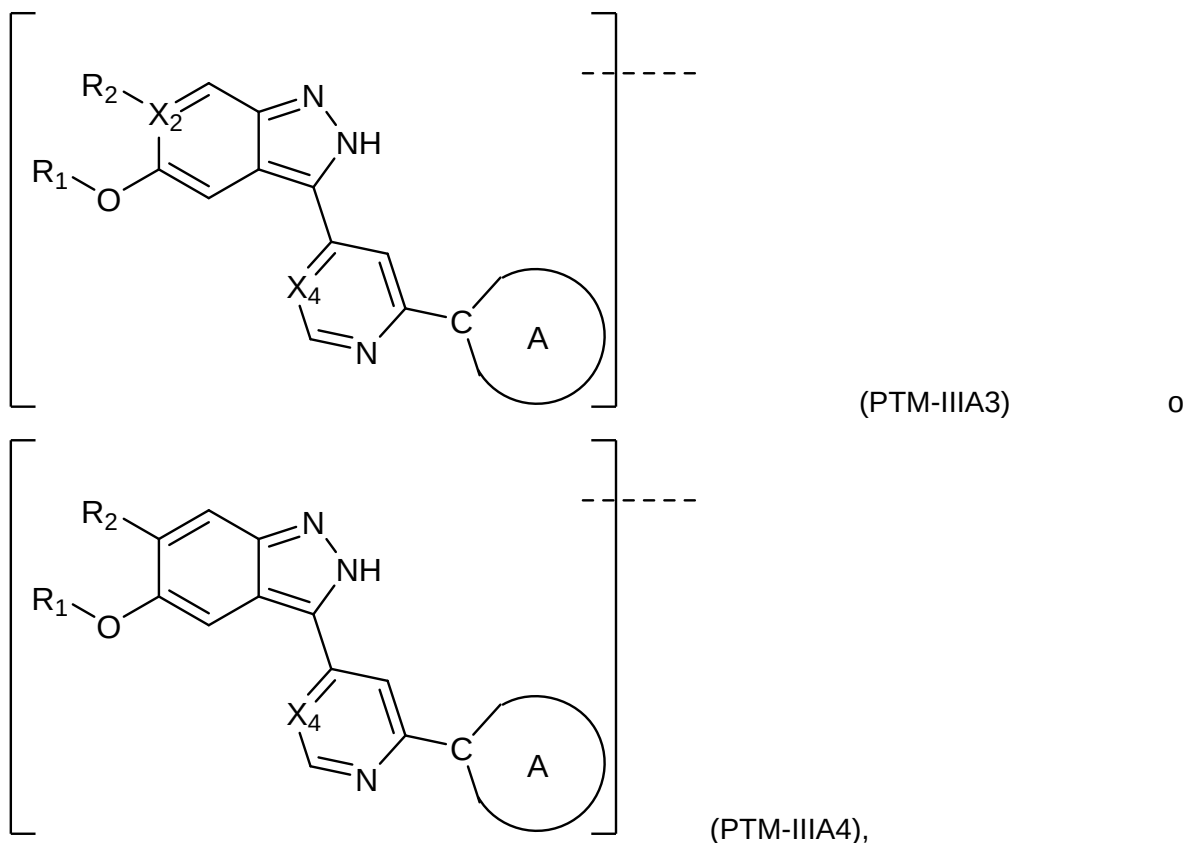
--- representa un enlace simple o un enlace doble; y

--- representa un enlace que puede ser estereoespecífico ((R) o (S)) o no

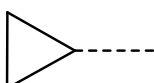
estereoespecífico;

(b) la PTM es un resto de direccionamiento a cinasa 2 repetida rica en leucina (LRRK2) de micromolécula que se une a LRRK2 o una forma mutante de este representado por la estructura química:





en donde:

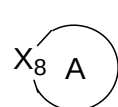
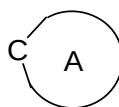
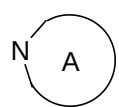
R_1 es un isopropilo, terc-butilo,  o , en donde  es el punto de unión al átomo de oxígeno de la PTM;

R_2 es hidrógeno, F, Cl, OH, alquilo C1-C3 o fluoroalquilo C1-C3;

X_6 y X_7 son cada uno independientemente CH o N;

X_1 , X_2 , X_3 , X_4 y X_5 son cada uno independientemente un N o CH que está opcionalmente sustituido con R_2 cuando CH;

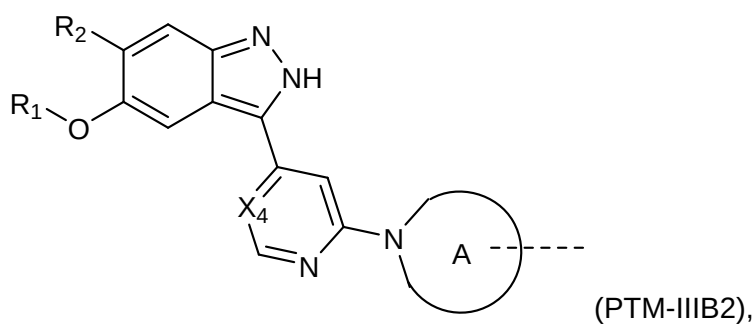
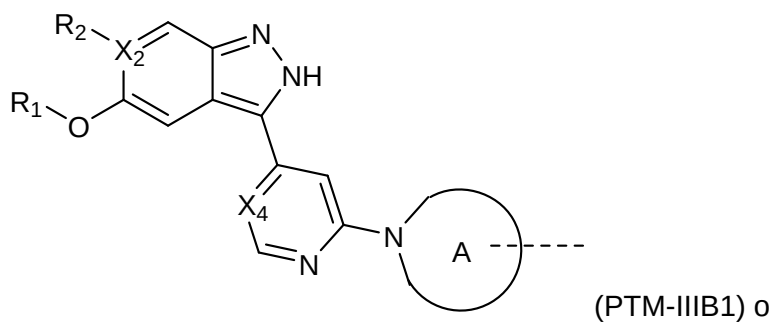
X_8 es CH o N;

,  o  es un cicloalquilo, heterocicloalquilo, bicicloalquilo, biheterocicloalquilo, espirocicloalquilo o espiroheterocicloalquilo de 3-10 miembros opcionalmente sustituido que contiene 1-4 (por ejemplo, 1, 2, 3 o 4) heteroátomos que se seleccionan de N, O y S (por ejemplo, opcionalmente sustituido con una o más (por ejemplo, 1, 2, 3 o 4) sustituciones; y

 del PTM indica el punto de unión con la L; y

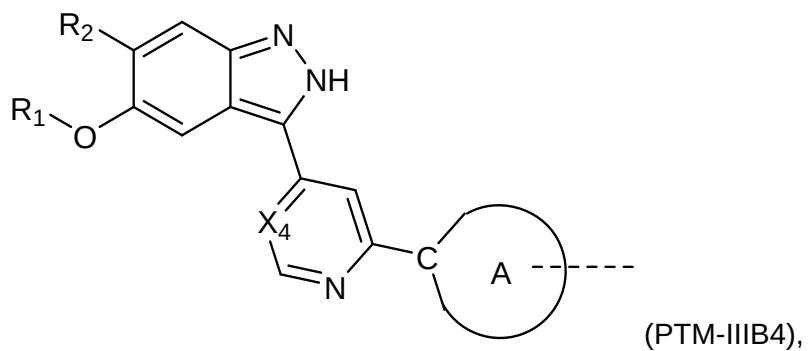
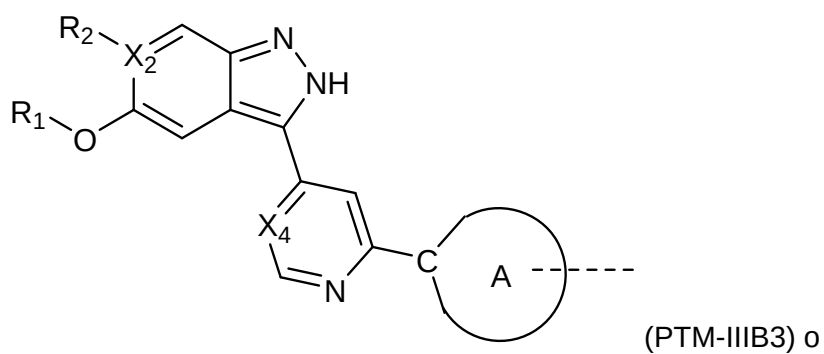
(c) la L es un enlace o un grupo enlazador químico que acopla covalentemente la CLM a la PTM.

5. El compuesto de la reivindicación 4, en donde la PTM está representada por:



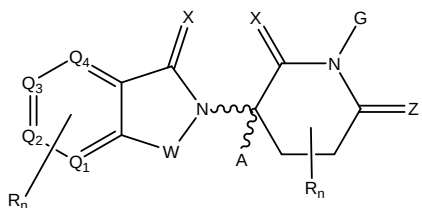
en --- donde el PTM indica el punto de unión con la L.

6. El compuesto de la reivindicación 4, en donde la PTM está representada por:

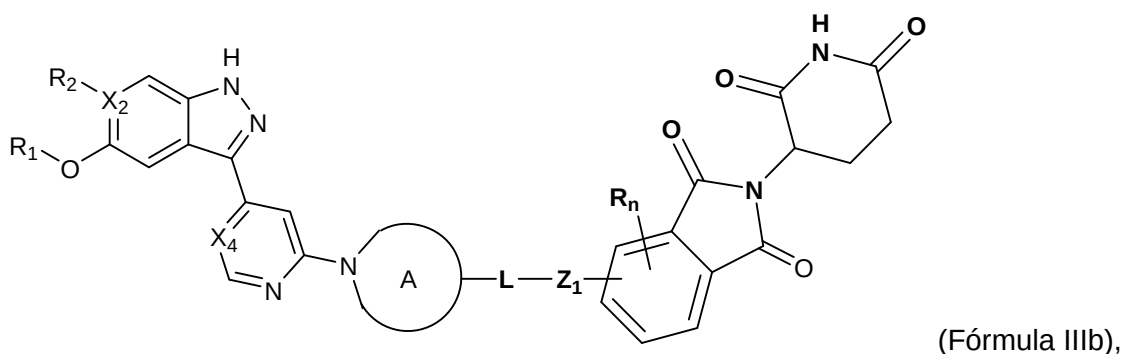
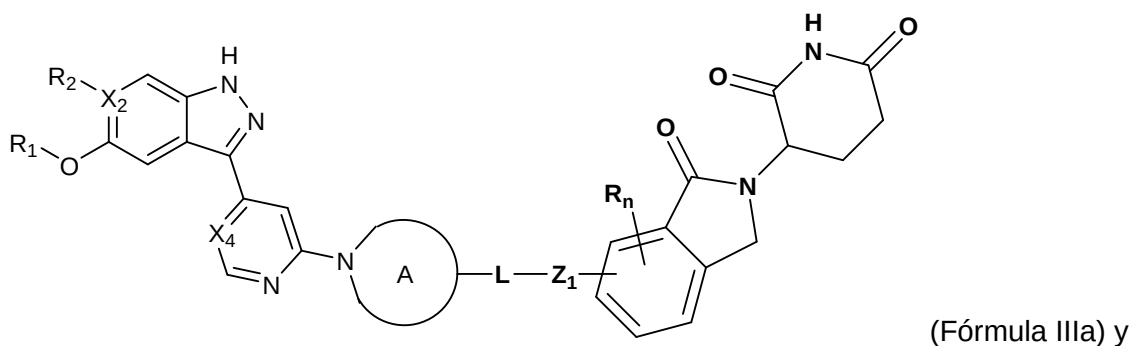
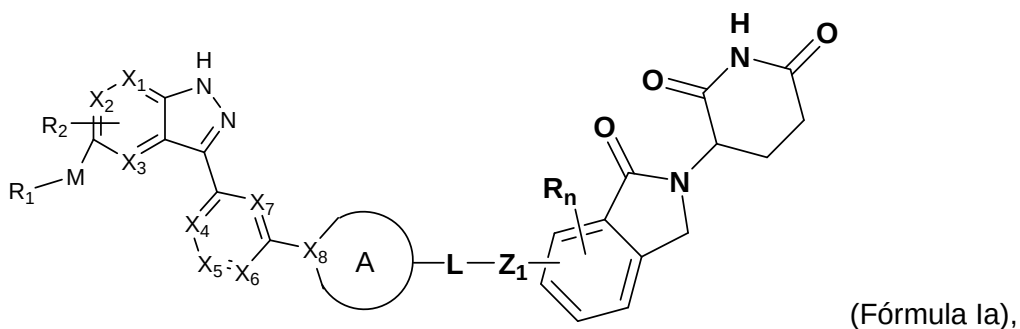


en --- donde el PTM indica el punto de unión con la L.

7. El compuesto de cualquiera de las reivindicaciones 1-7, en donde la CLM está representada por la estructura química:



8. El compuesto de cualquiera de las reivindicaciones 1-7, en donde el compuesto está representado por una estructura química que se selecciona de:



en donde:

X₂ es C, CH o N;

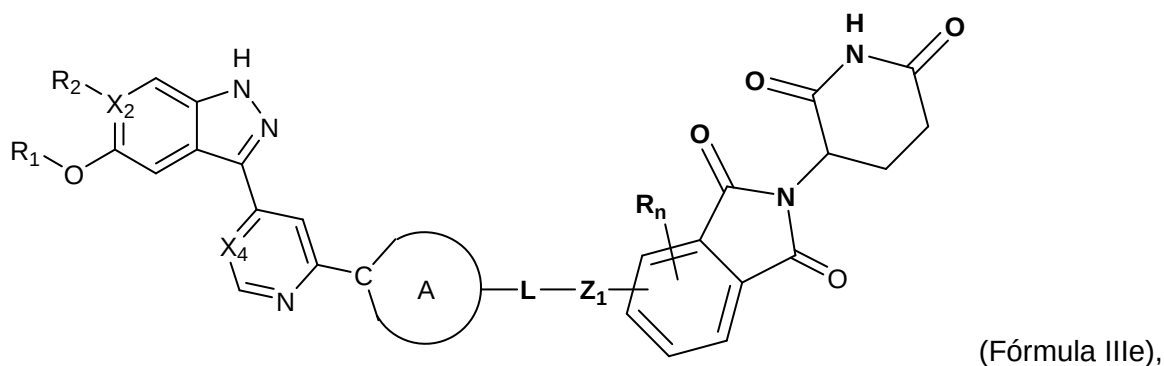
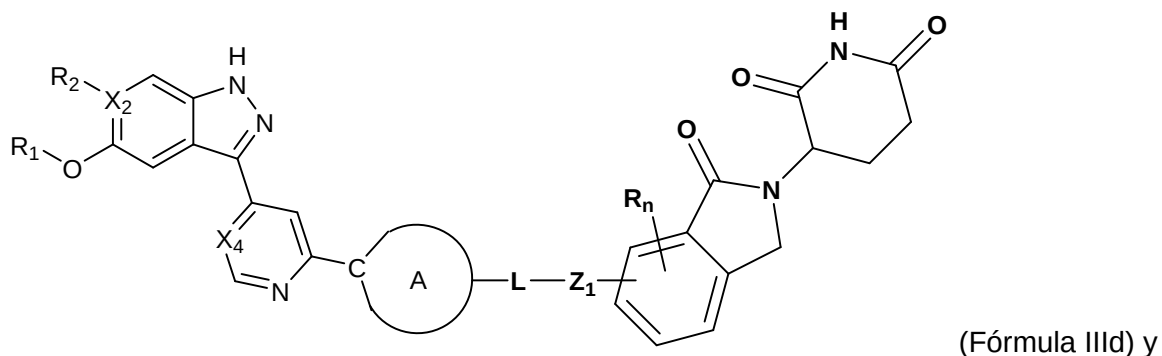
Z₁ es un enlace, un carbono compartido con un grupo cíclico de L o un nitrógeno compartido con un grupo cíclico de L;

n es un número entero de 0 a 3 (por ejemplo, 0, 1, 2 o 3);

R es un enlace, H, O, OH, N, NH, NH₂, Cl, -F, metilo, metoxi o etoxi; y

R² es H, Cl, F, OH, alquilo C1-C3 o fluoralquilo C1-3.

9. El compuesto de cualquiera de las reivindicaciones 1-7, en donde el compuesto está representado por una estructura química que se selecciona de:



en donde:

X₂ es C, CH o N;

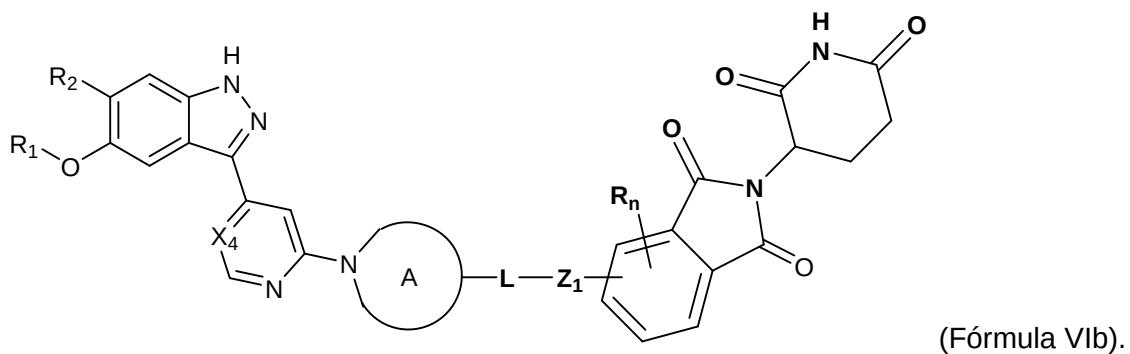
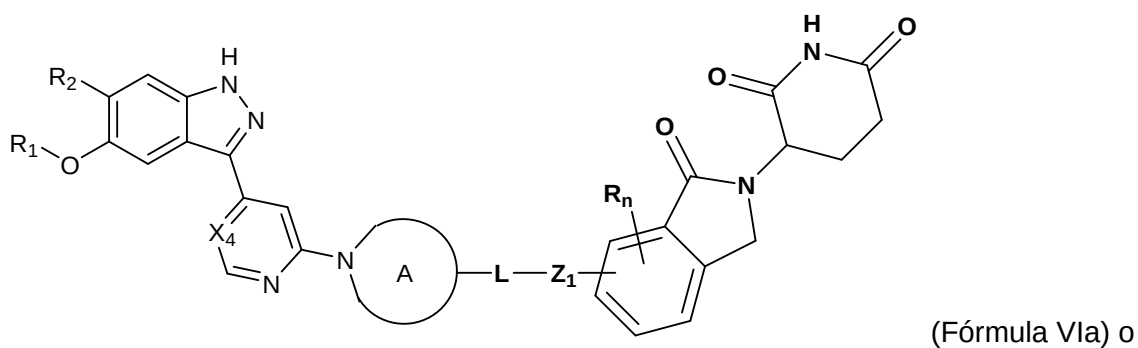
Z₁ es un enlace, un carbono compartido con un grupo cíclico de L o un nitrógeno compartido con un grupo cíclico de L;

n es un número entero de 0 a 3 (por ejemplo, 0, 1, 2 o 3);

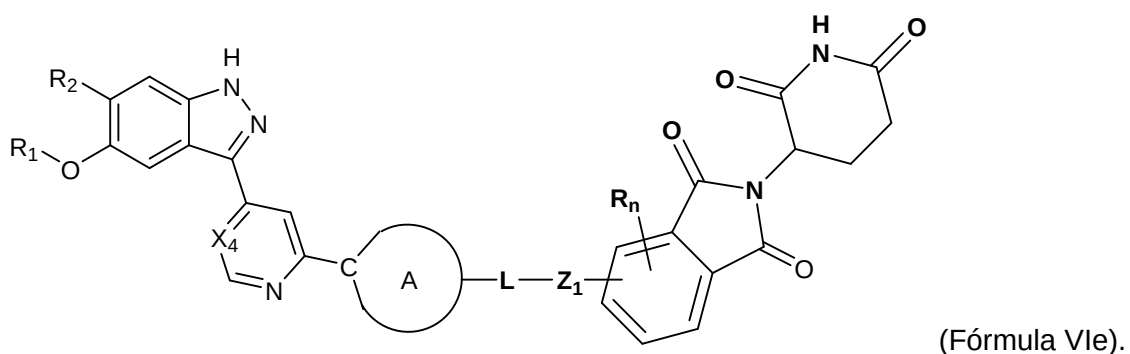
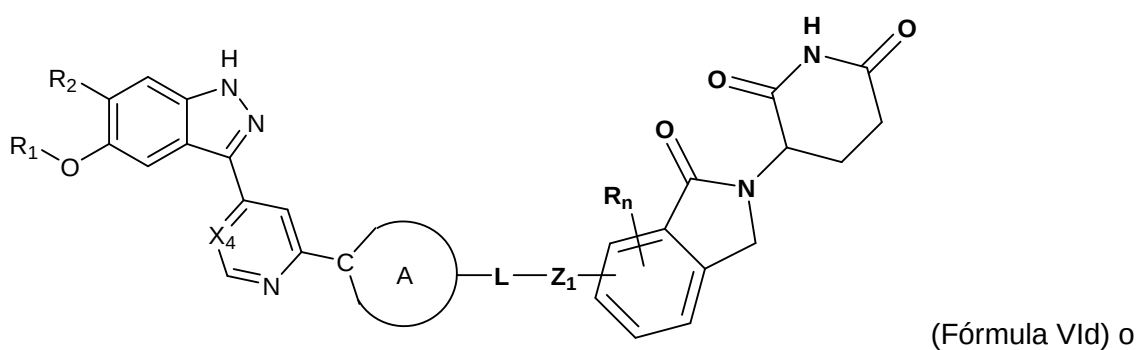
R es un enlace, H, O, OH, N, NH, NH₂, Cl, -F, metilo, metoxi o etoxi; y

R² es H, Cl, F, OH, alquilo C1-C3 o fluoralquilo C1-3.

10. El compuesto de la reivindicación 10, en donde el compuesto está representado por la estructura química:



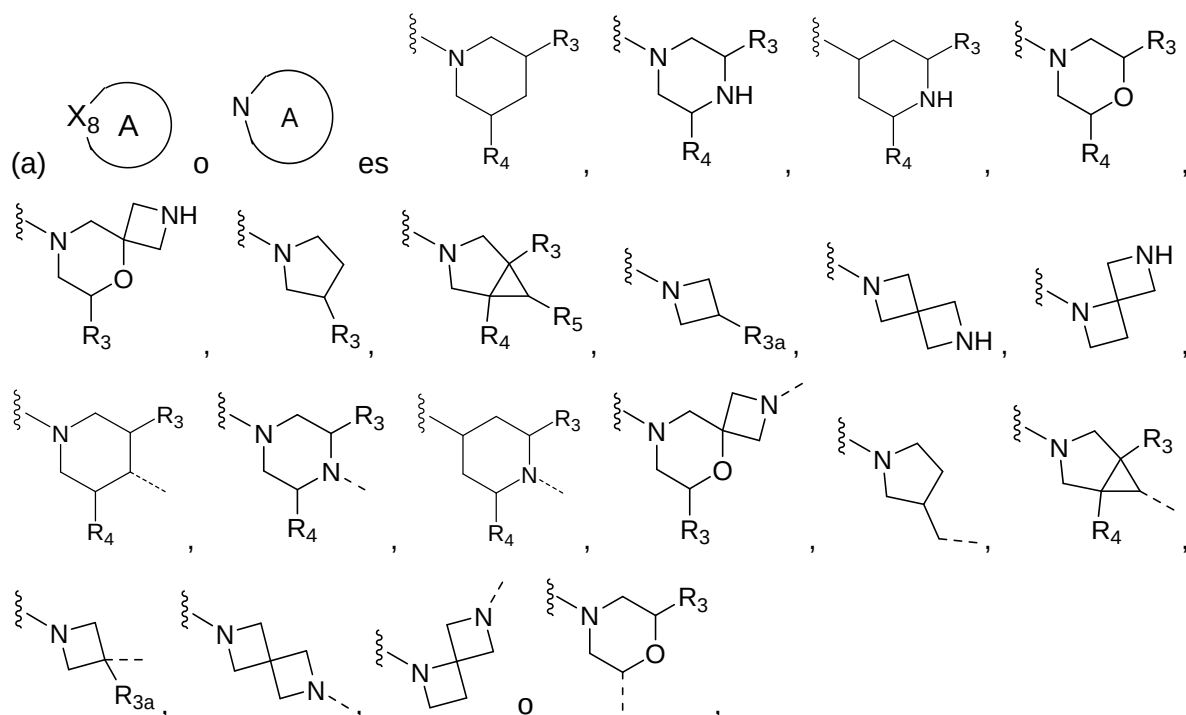
11. El compuesto de la reivindicación 10, en donde el compuesto está representado por la estructura química:



12. El compuesto de cualquiera de las reivindicaciones 1-11, en donde cada R se selecciona de un H, O, OH, NH, NH₂, -Cl, -F, CN, CF₃, alquilo C₁₋₃ lineal o ramificado opcionalmente sustituido, alcoxi C₁₋₃ lineal o ramificado opcionalmente sustituido.

13. El compuesto de cualquiera de las reivindicaciones 1-11, en donde cada R se selecciona de un H, O, OH, NH, NH₂, -Cl, -F, -CN, CF₃, metilo, metoxi y etoxi.

14. El compuesto de cualquiera de las reivindicaciones 1-13, en donde:



en donde:

R₃ es H o metilo;

R_{3a} es H, halógeno o metilo;

R₄ es H o metilo;

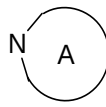
R₅ es H o metilo;

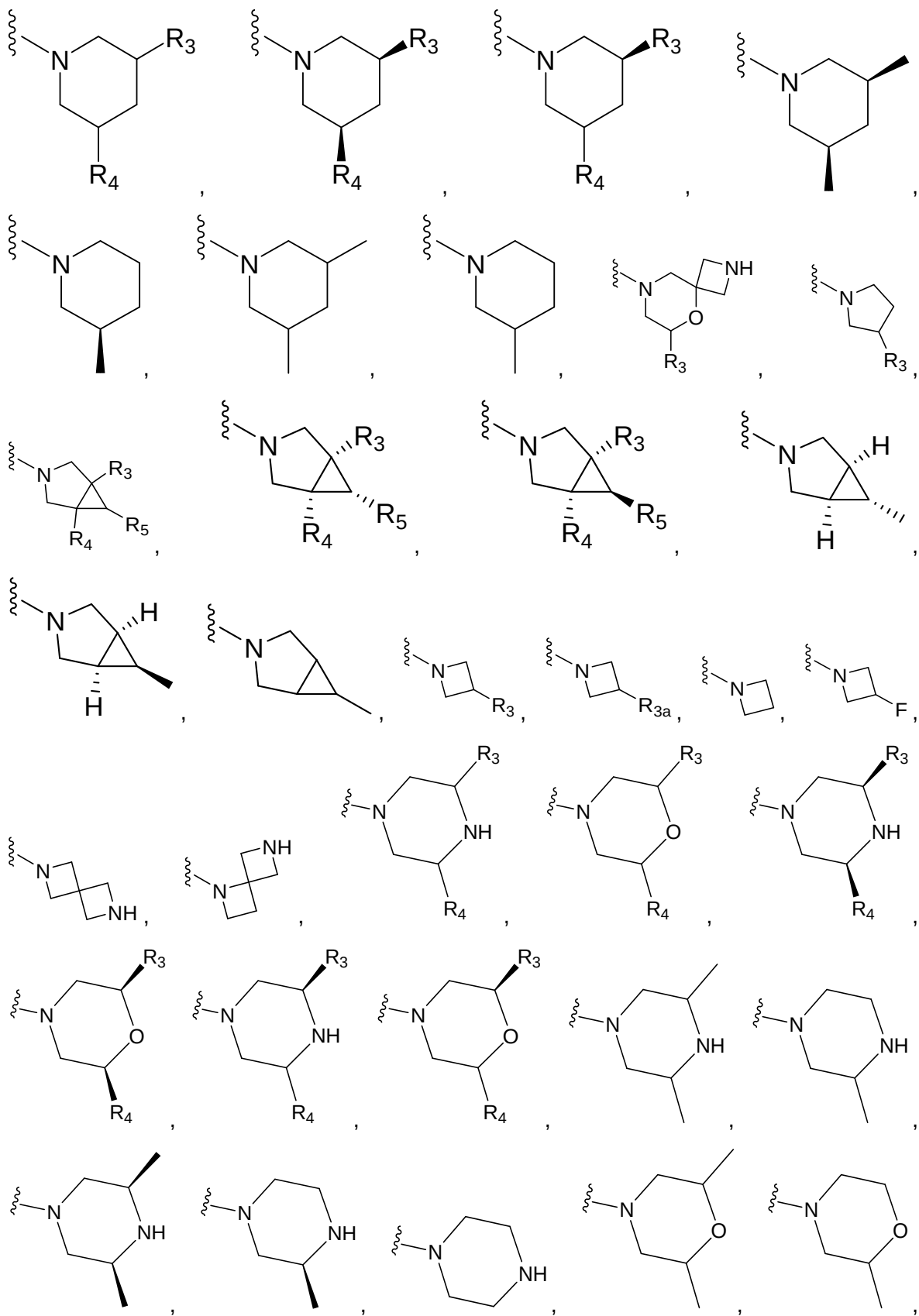
 indica el punto de unión al PTM; y

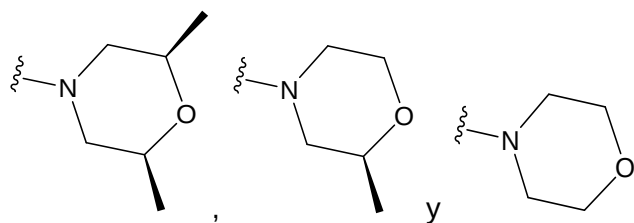
 indica el punto de unión con la L, y donde  no está presente, la  está unida a la L a través de un átomo de un N o CH del grupo cíclico, R₃, R₄ o R₅;

(b) R₂ es H o F; o

(c) una combinación de estos.

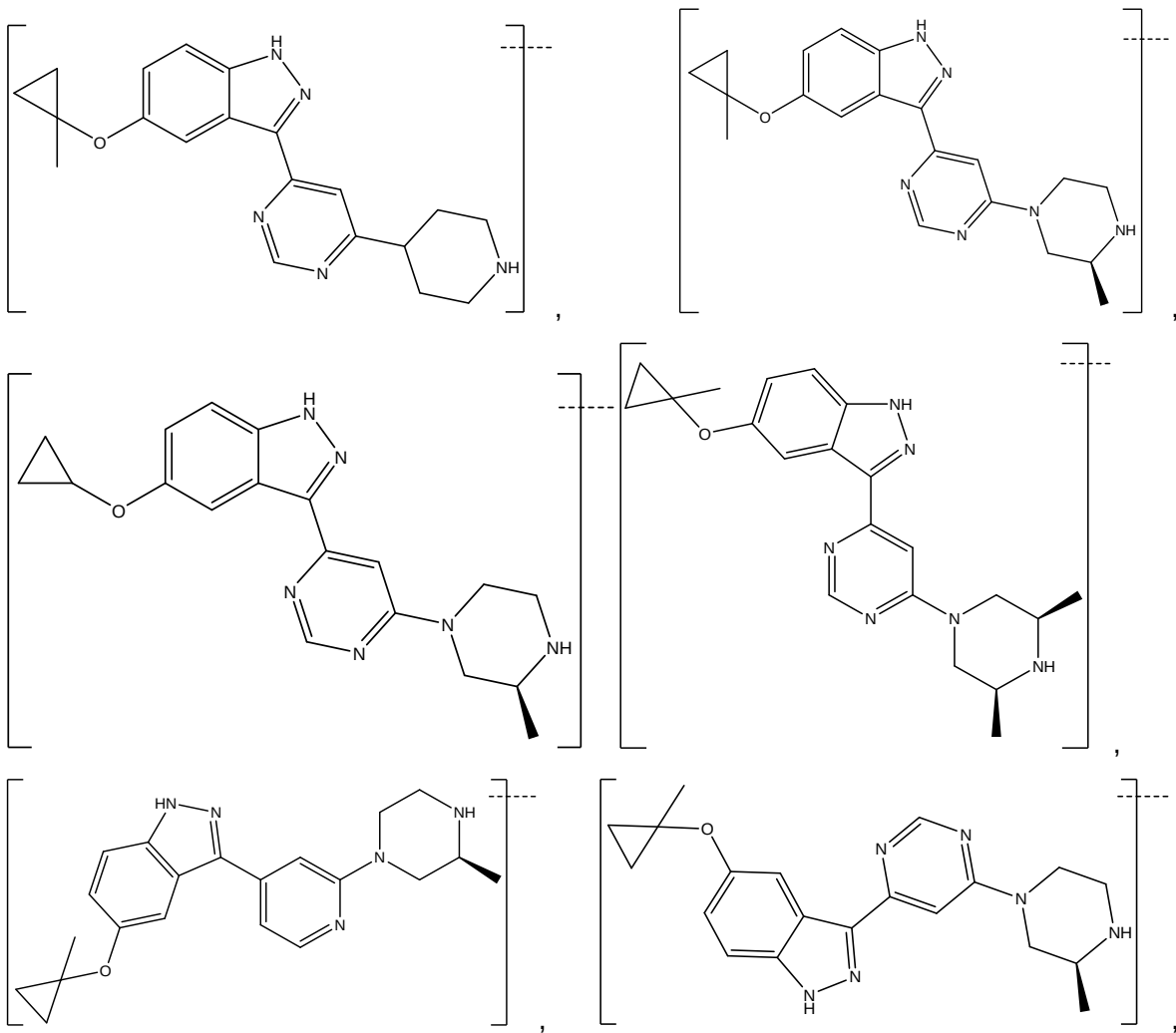
15. El compuesto de cualquiera de las reivindicaciones 1-14, en donde  se selecciona del grupo que consiste en:

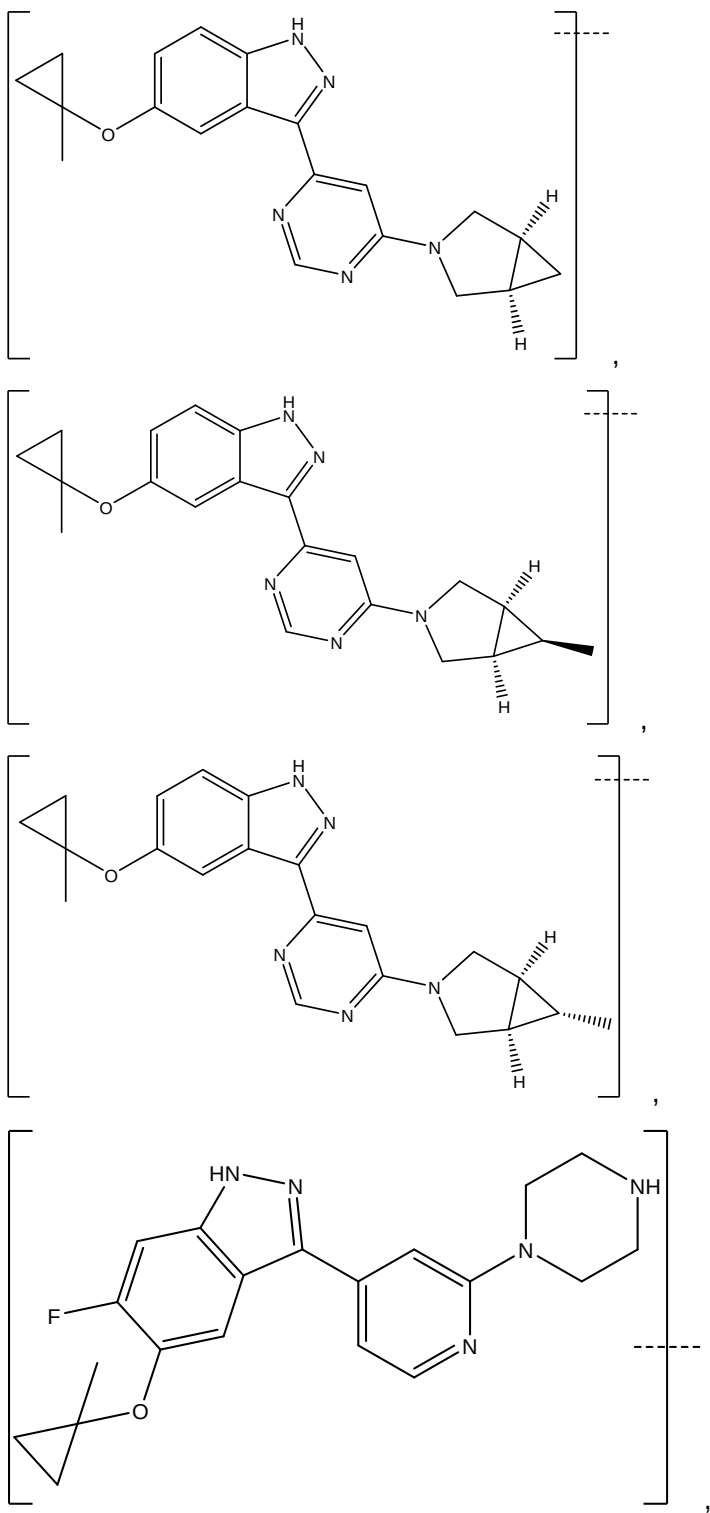


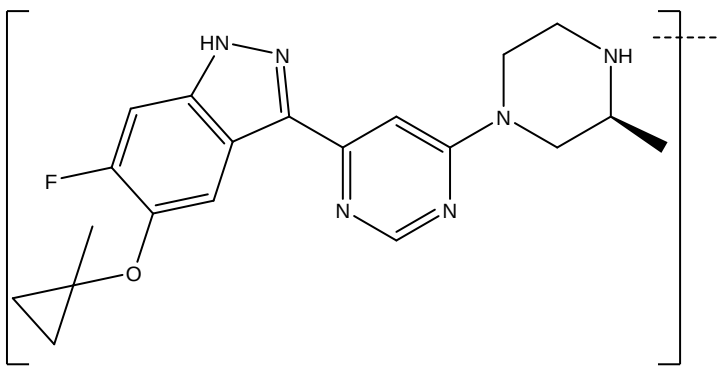
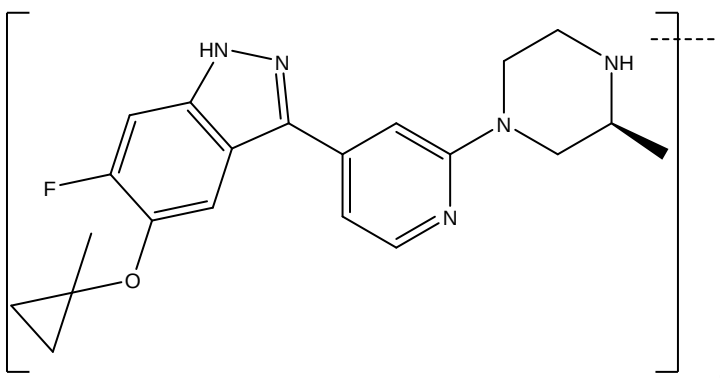
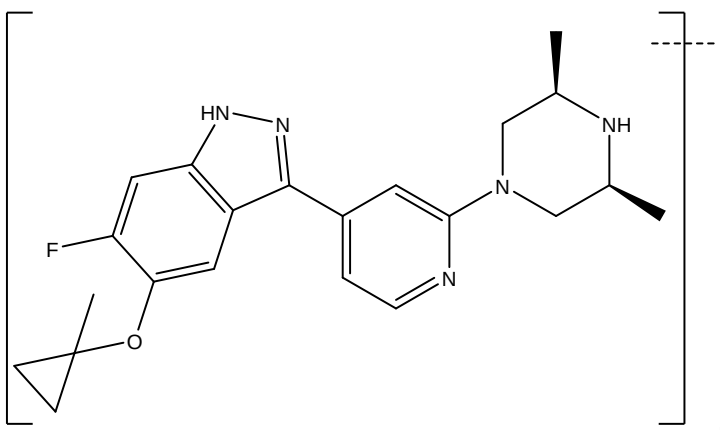
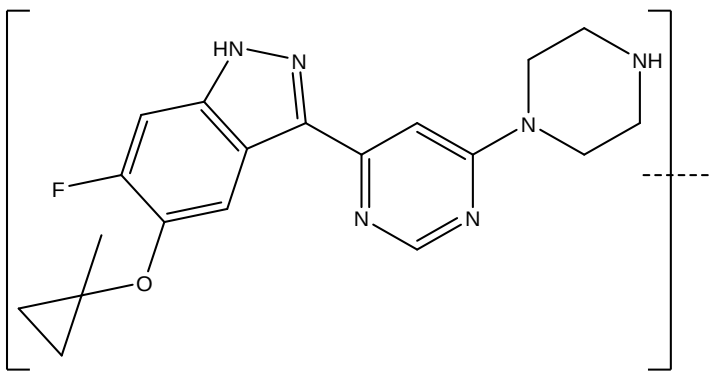


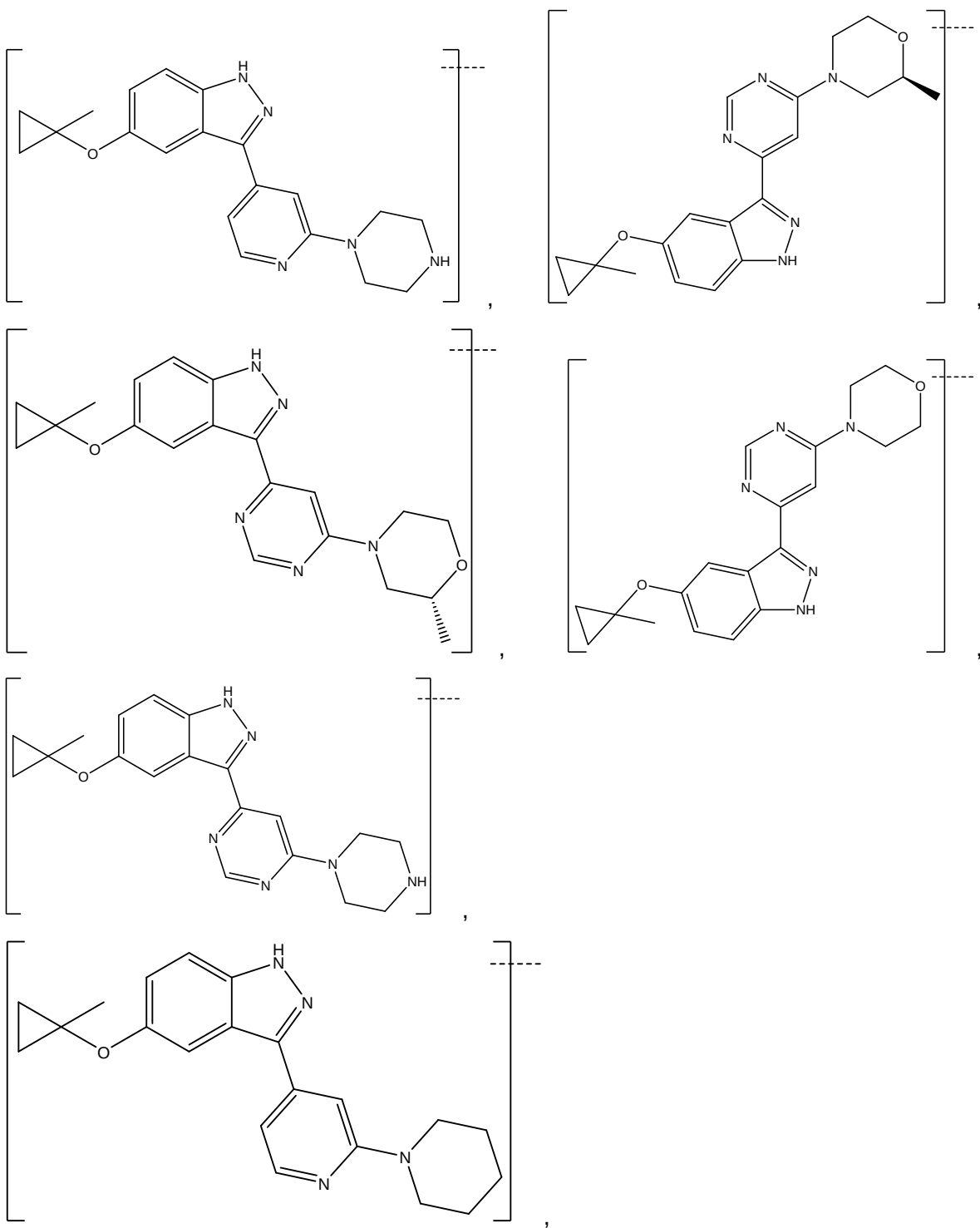
, y , en donde el heterocicloalquilo está unido a la L o la PTM a través de un átomo del grupo cíclico o un sustituyente de este.

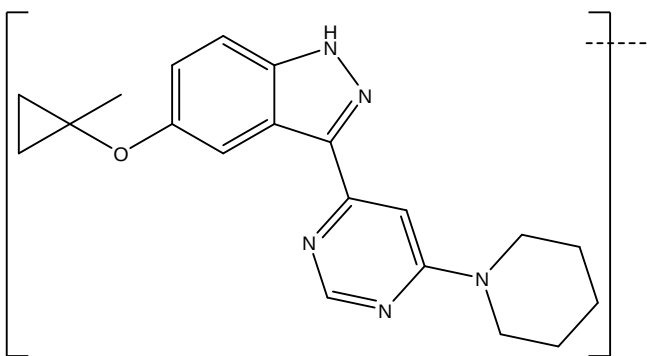
16. El compuesto de cualquiera de las reivindicaciones 1-13, en donde la PTM está representada por una estructura química:



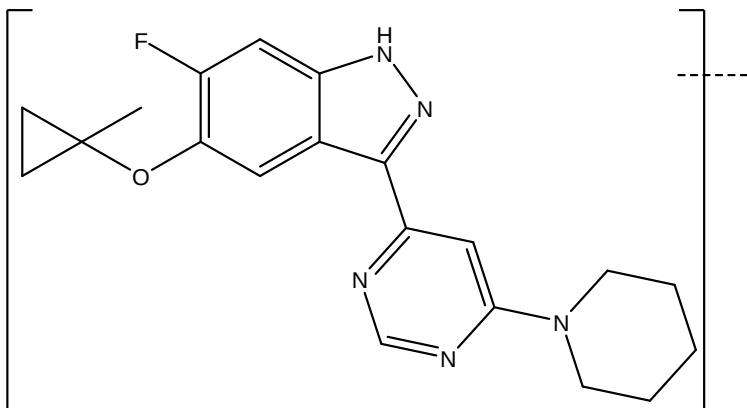




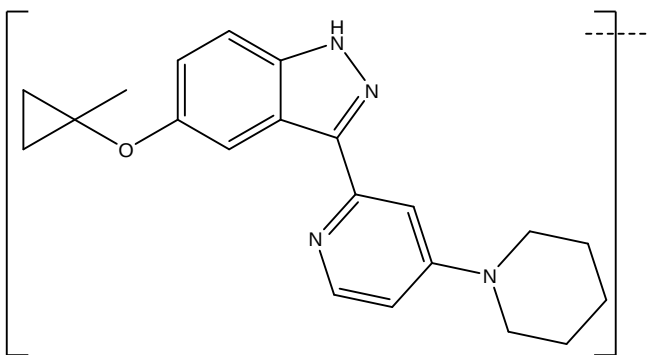




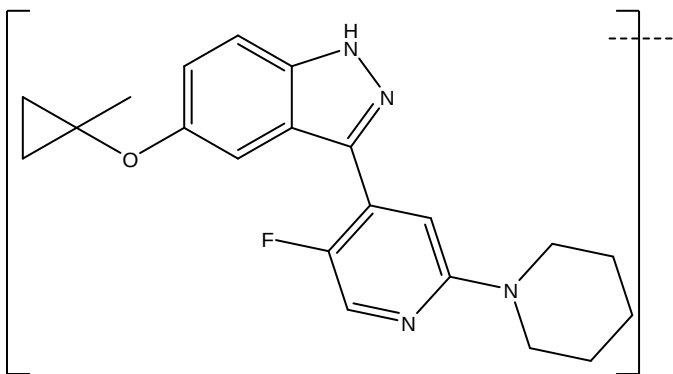
,



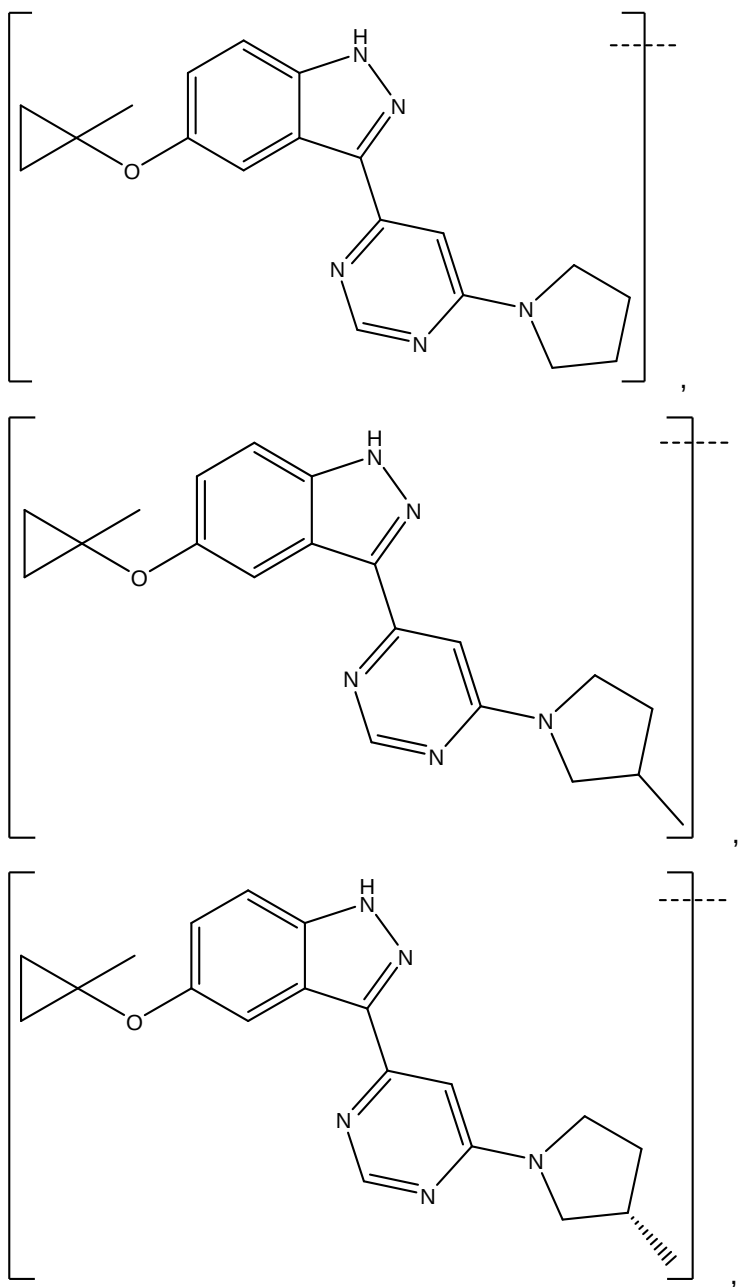
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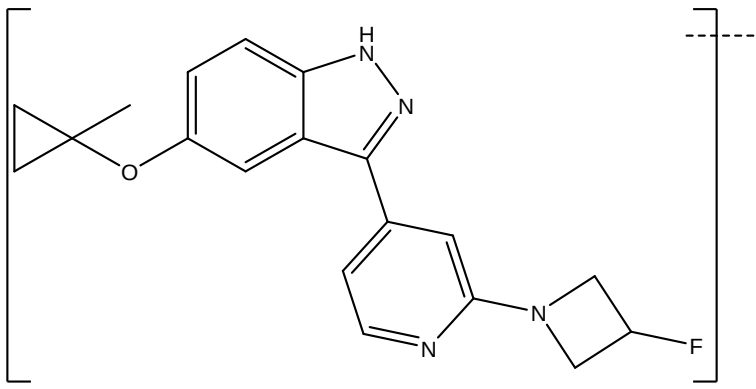
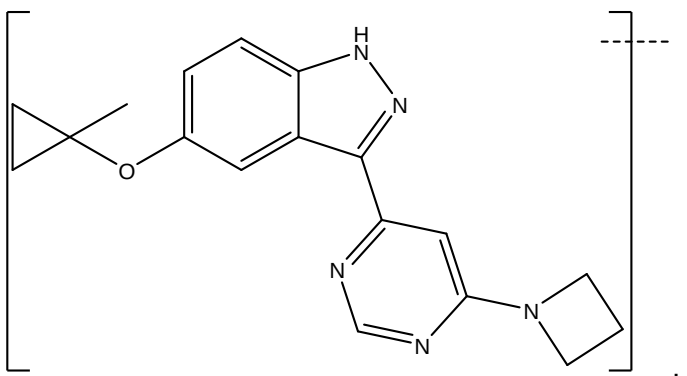
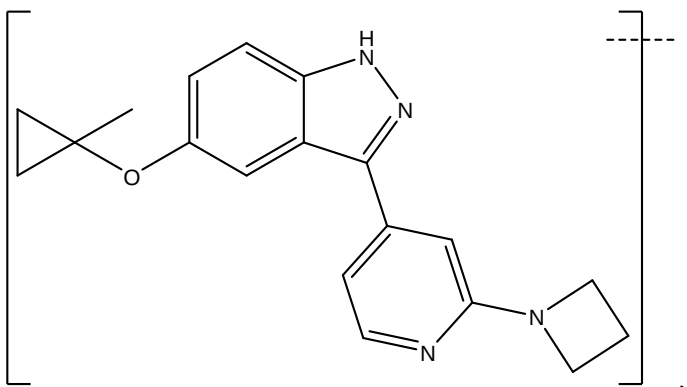
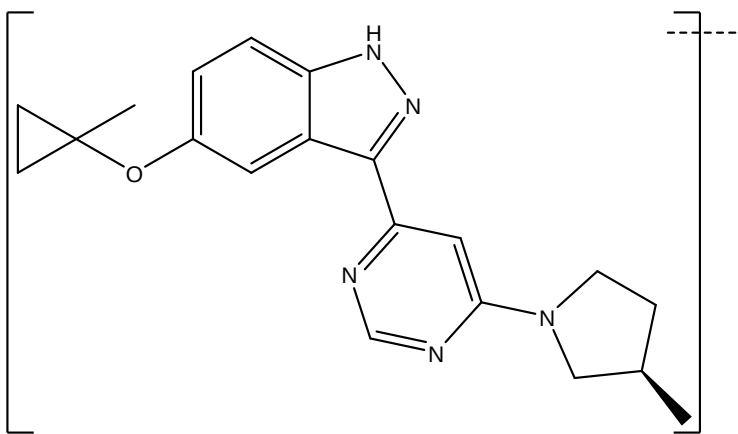


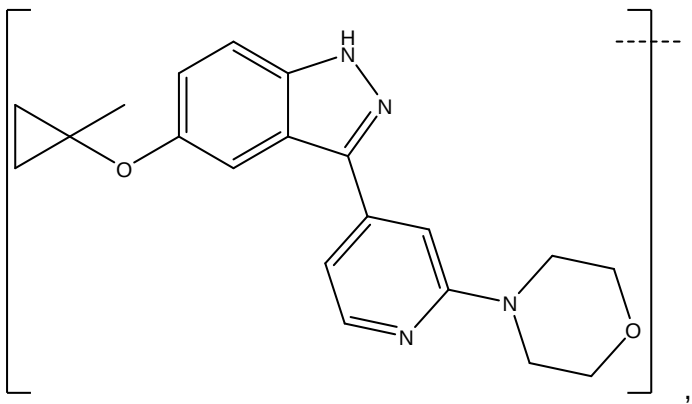
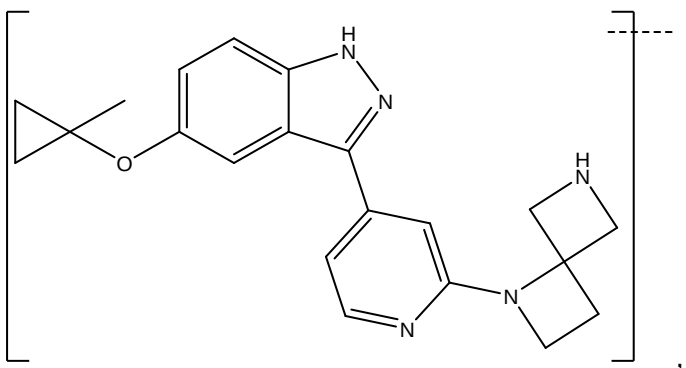
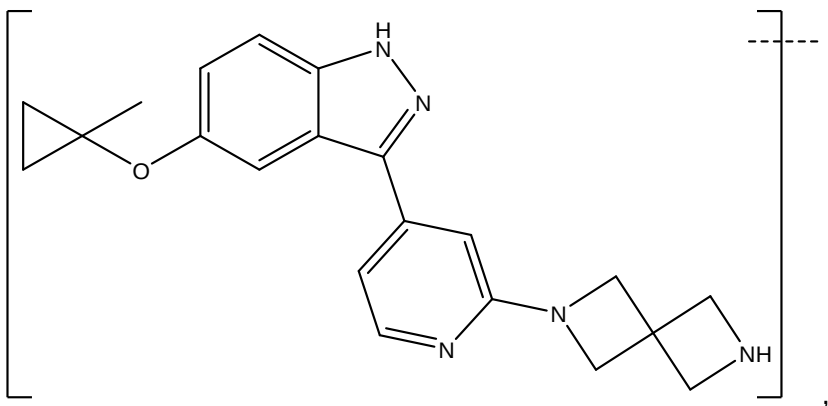
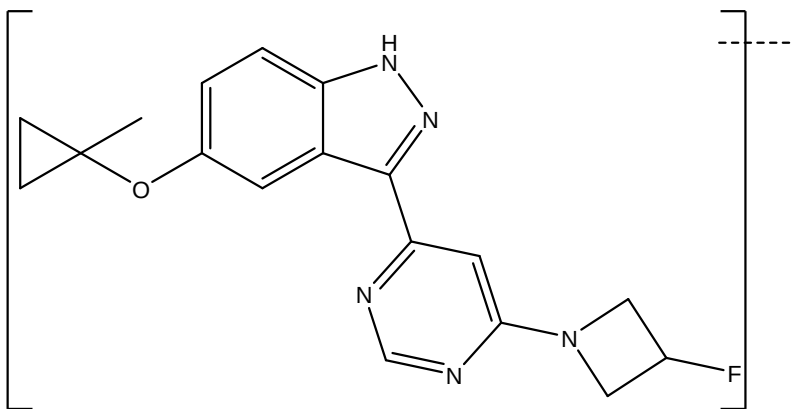
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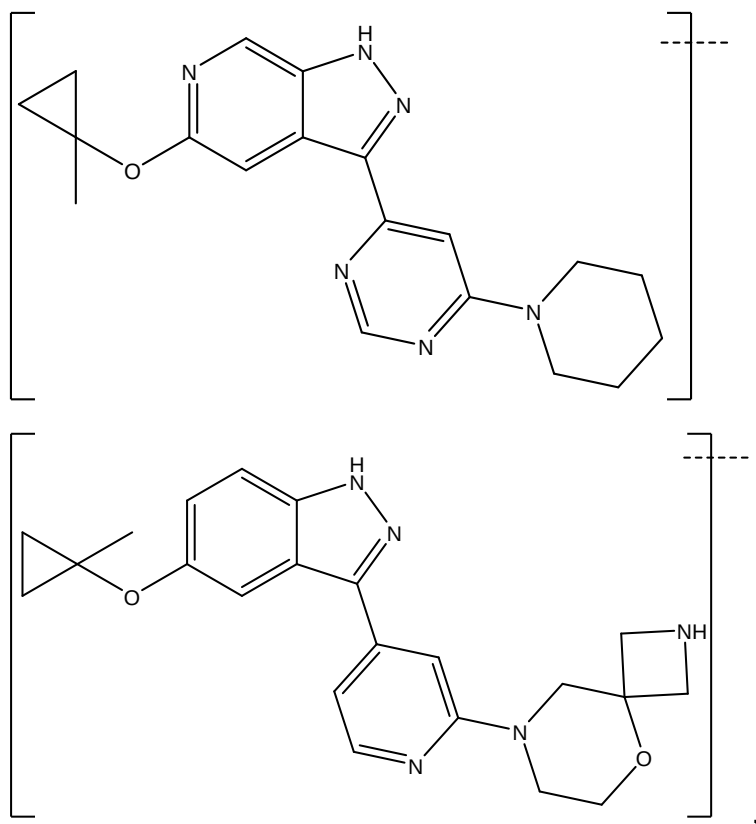


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en donde indica un sitio de unión de la L.

17. El compuesto de cualquiera de las reivindicaciones 1-16, en donde L comprende una unidad estructural química representada por la fórmula:

$$-(A^L)_q^- \text{ ,}$$

en donde:

$-(A^L)_q$ - es un grupo que está conectado al CLM y al PTM;

q es un número entero igual o superior a 1;

cada A^L se selecciona independientemente de CR^{L1}R^{L2}, O, S, SO, SO₂, NR^{L3}, SO₂NR^{L3}, SONR^{L3}, CONR^{L3}, NR^{L3}CONR^{L4}, NR^{L3}SO₂NR^{L4}, CO, CR^{L1}=CR^{L2}, C≡C, cicloalquilo C₃₋₁₁ opcionalmente sustituido con 1-6 grupos R^{L1} y/o R^{L2}, espirocicloalquilo C₅₋₁₃ opcionalmente sustituido con 1-9 grupos R^{L1} y/o R^{L2}, heteociclilo C₃₋₁₁ opcionalmente sustituido con 1-6 grupos R^{L1} y/o R^{L2}, espiroheterociclilo C₅₋₁₃ opcionalmente sustituido con 1-8 grupos R^{L1} y/o R^{L2}, arilo opcionalmente sustituido con 0-6 grupos R^{L1} y/o R^{L2}, y heteroarilo opcionalmente sustituido con 1-6 grupos R^{L1} y/o R^{L2}; y

R^{L1}, R^{L2}, R^{L3}, R^{L4} y R^{L5} son, cada uno independientemente, H, halógeno, C₁₋₈alquilo, OC₁₋₈alquilo, SC₁₋₈alquilo, NHC₁₋₈alquilo, N(C₁₋₈alquilo)₂, C₃₋₁₁cicloalquilo, arilo, heteroarilo, C₃₋

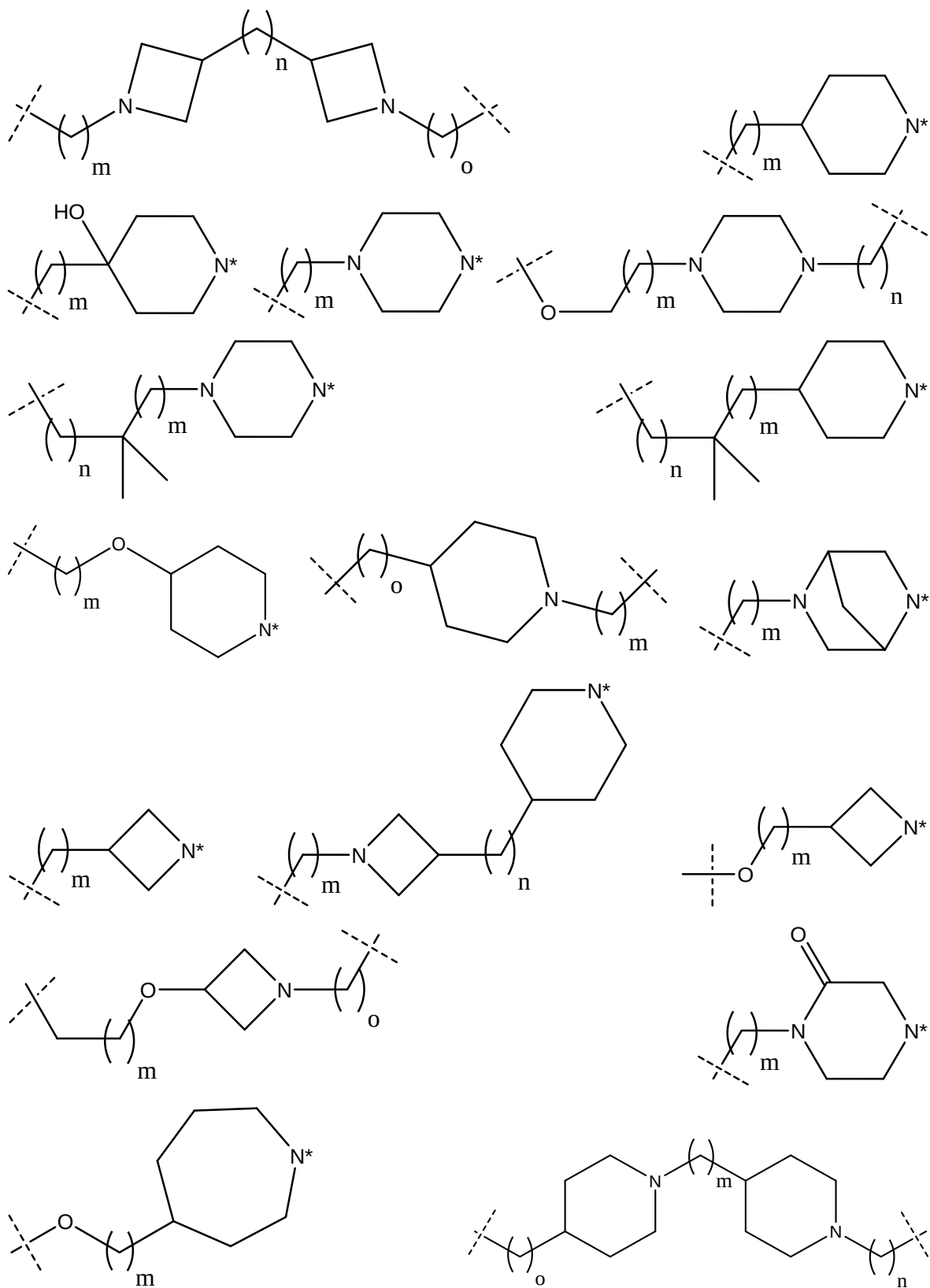
₁₁heterociclilo, OC₃₋₈cicloalquilo, SC₃₋₈cicloalquilo, NHC₃₋₈cicloalquilo, N(C₃₋₈cicloalquilo)₂, N(C₃₋₈cicloalquilo)(C₁₋₈alquilo), OH, NH₂, SH, SO₂C₁₋₈alquilo, P(O)(OC₁₋₈alquilo)(C₁₋₈alquilo), P(O)(OC₁₋₈alquilo)₂, CC-C₁₋₈alquilo, CCH, CH=CH(C₁₋₈alquilo), C(C₁₋₈alquilo)=CH(C₁₋₈alquilo), C(C₁₋₈alquilo)=C(C₁₋₈alquilo)₂, Si(OH)₃, Si(C₁₋₈alquilo)₃, Si(OH)(C₁₋₈alquilo)₂, COC₁₋₈alquilo, CO₂H, CN, CF₃, CHF₂, CH₂F, NO₂, SF₅, SO₂NHC₁₋₈alquilo, SO₂N(C₁₋₈alquilo)₂, SONHC₁₋₈alquilo, SON(C₁₋₈alquilo)₂, CONHC₁₋₈alquilo, CON(C₁₋₈alquilo)₂, N(C₁₋₈alquilo)CONH(C₁₋₈alquilo), N(C₁₋₈alquilo)CON(C₁₋₈alquilo)₂, NHCONH(C₁₋₈alquilo), NHCON(C₁₋₈alquilo)₂, NHCONH₂, N(C₁₋₈alquilo)SO₂NH(C₁₋₈alquilo), N(C₁₋₈alquilo)SO₂N(C₁₋₈alquilo)₂, NH SO₂NH(C₁₋₈alquilo), NH SO₂N(C₁₋₈alquilo)₂ o NH SO₂NH₂.

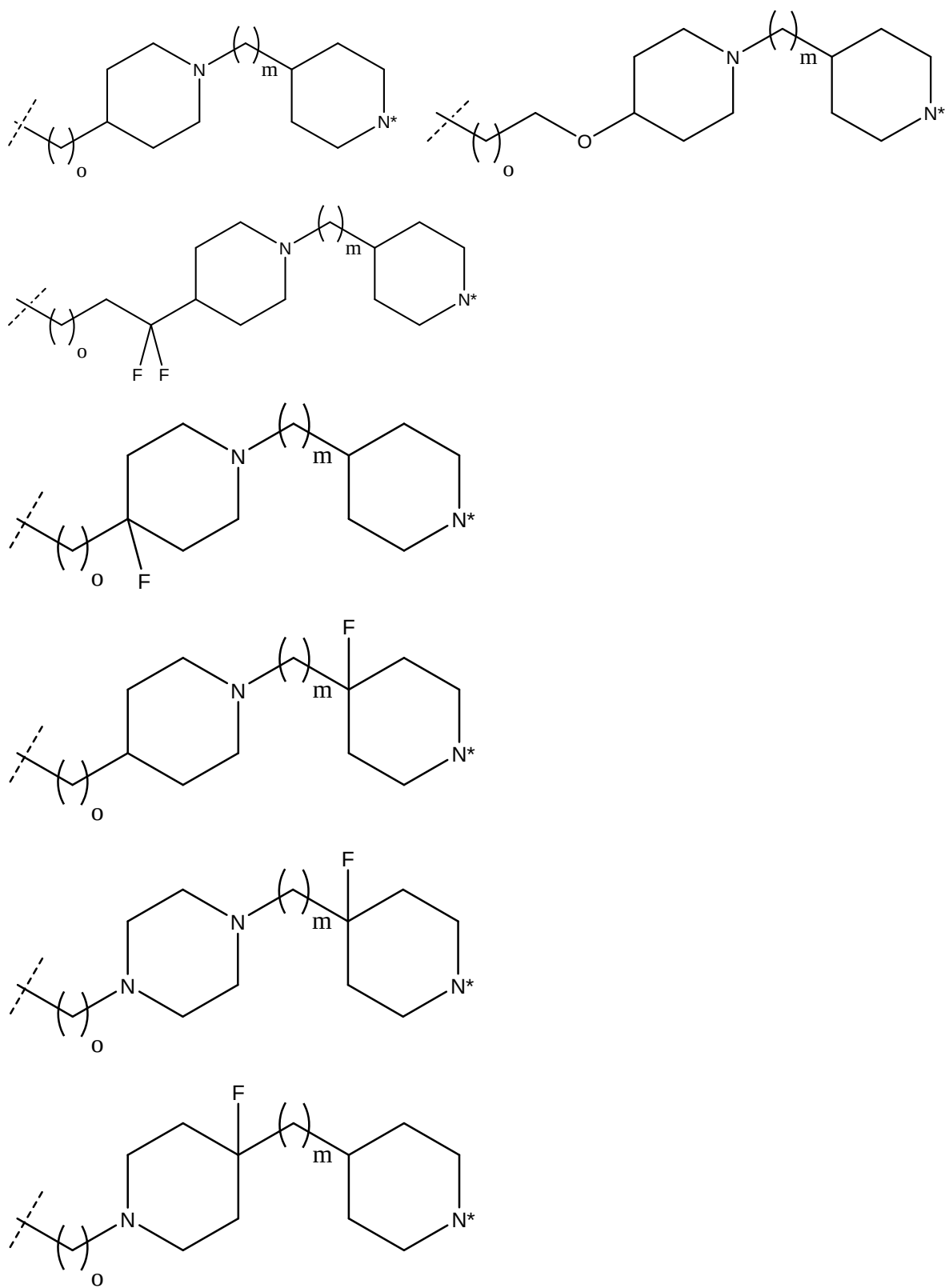
18. El compuesto de cualquiera de las reivindicaciones 1-16, en donde L incluye un alquilo C₁-C₅₀ opcionalmente sustituido (por ejemplo, alquilo C₁, C₂, C₃, C₄, C₅, C₆, C₇, C₈, C₉, C₁₀, C₁₁, C₁₂, C₁₃, C₁₄, C₁₅, C₁₆, C₁₇, C₁₈, C₁₉, C₂₀, C₂₁, C₂₂, C₂₃, C₂₄, C₂₅, C₂₆, C₂₇, C₂₈, C₂₉, C₃₀, C₃₁, C₃₂, C₃₃, C₃₄, C₃₅, C₃₆, C₃₇, C₃₈, C₃₉, C₄₀, C₄₁, C₄₂, C₄₃, C₄₄, C₄₅, C₄₆, C₄₇, C₄₈, C₄₉ o C₅₀), en donde:

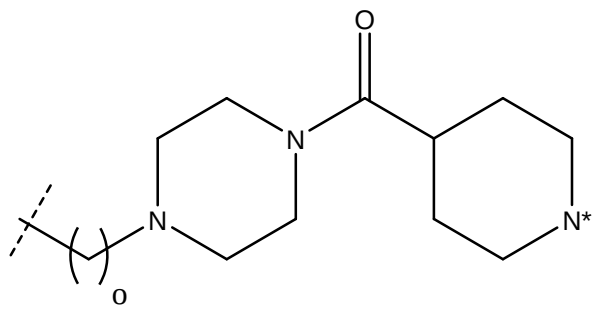
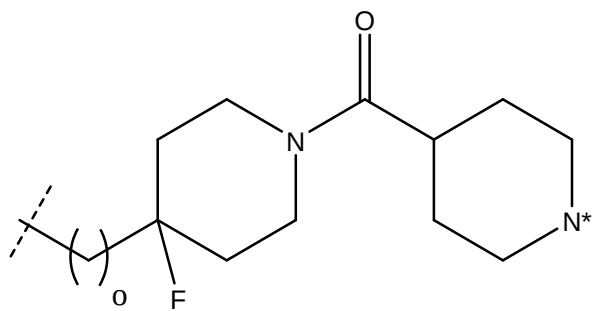
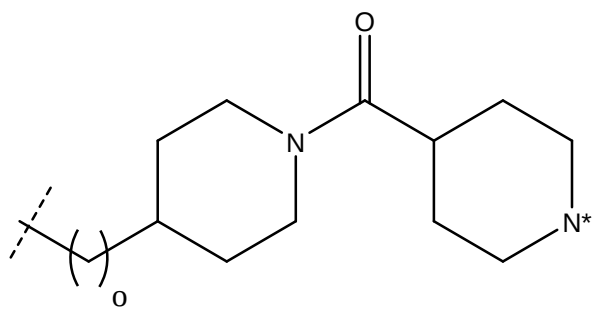
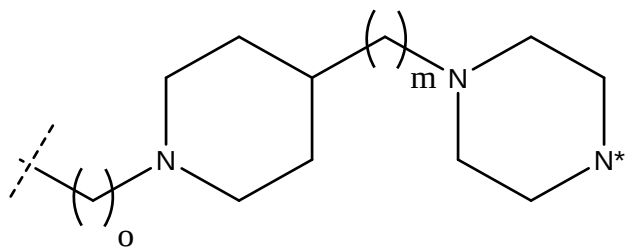
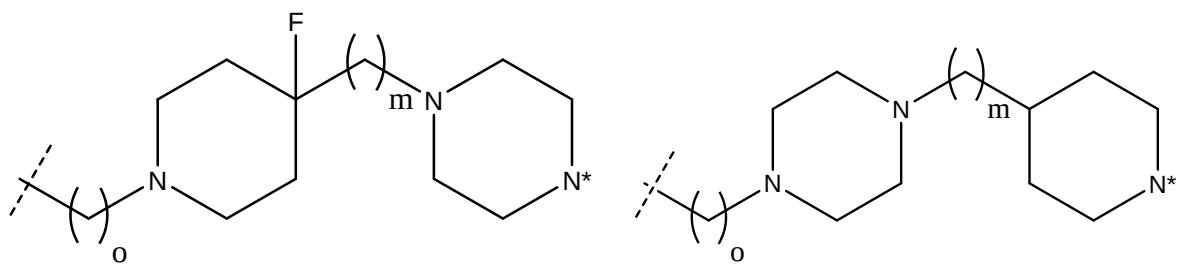
cada carbono se reemplaza opcionalmente con CR^{L1}R^{L2}, O, S, SO, SO₂, NR^{L3}, SO₂NR^{L3}, SONR^{L3}, CONR^{L3}, NR^{L3}CONR^{L4}, NR^{L3}SO₂NR^{L4}, CO, CR^{L1}=CR^{L2}, C≡C, cicloalquilo C₃₋₁₁ opcionalmente sustituido con 1-6 grupos R^{L1} y/o R^{L2}, espirocicloalquilo C₅₋₁₃ opcionalmente sustituido con 1-9 grupos R^{L1} y/o R^{L2}, heteociclilo C₃₋₁₁ opcionalmente sustituido con 1-6 grupos R^{L1} y/o R^{L2}, espiroheterociclilo C₅₋₁₃ opcionalmente sustituido con 1-8 grupos R^{L1} y/o R^{L2}, arilo opcionalmente sustituido con 1-6 grupos R^{L1} y/o R^{L2}, o heteroarilo opcionalmente sustituido con 1-6 grupos R^{L1} y/o R^{L2}; y

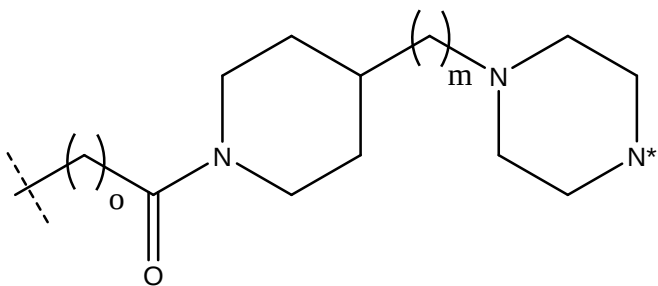
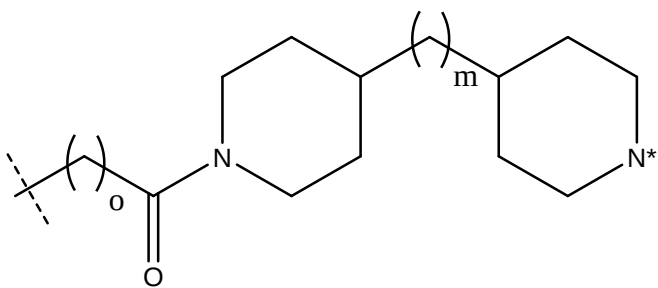
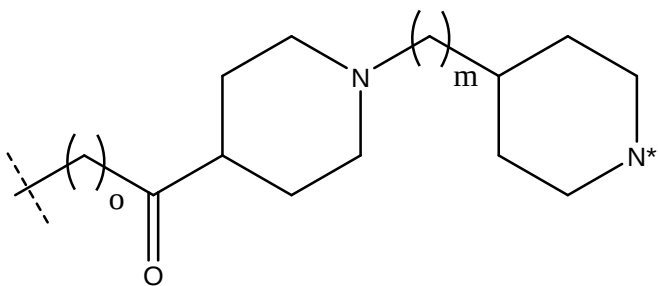
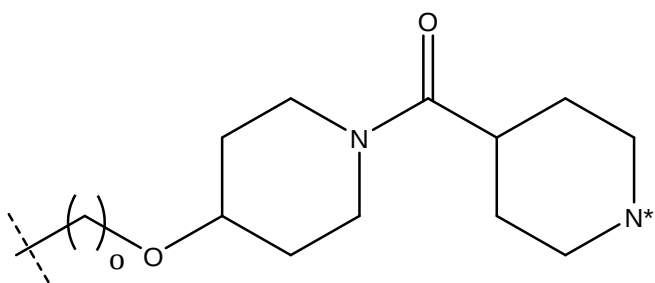
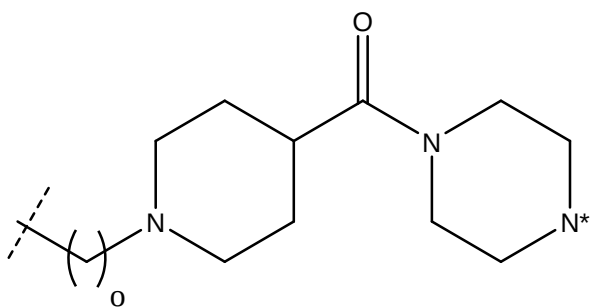
R^{L1}, R^{L2}, R^{L3}, R^{L4} y R^{L5} son, cada uno independientemente, H, halógeno, C₁₋₈alquilo, OC₁₋₈alquilo, SC₁₋₈alquilo, NHC₁₋₈alquilo, N(C₁₋₈alquilo)₂, C₃₋₁₁cicloalquilo, arilo, heteroarilo, C₃₋₁₁heterociclilo, OC₃₋₈cicloalquilo, SC₃₋₈cicloalquilo, NHC₃₋₈cicloalquilo, N(C₃₋₈cicloalquilo)₂, N(C₃₋₈cicloalquilo)(C₁₋₈alquilo), OH, NH₂, SH, SO₂C₁₋₈alquilo, P(O)(OC₁₋₈alquilo)(C₁₋₈alquilo), P(O)(OC₁₋₈alquilo)₂, CC-C₁₋₈alquilo, CCH, CH=CH(C₁₋₈alquilo), C(C₁₋₈alquilo)=CH(C₁₋₈alquilo), C(C₁₋₈alquilo)=C(C₁₋₈alquilo)₂, Si(OH)₃, Si(C₁₋₈alquilo)₃, Si(OH)(C₁₋₈alquilo)₂, COC₁₋₈alquilo, CO₂H, CN, CF₃, CHF₂, CH₂F, NO₂, SF₅, SO₂NHC₁₋₈alquilo, SO₂N(C₁₋₈alquilo)₂, SONHC₁₋₈alquilo, SON(C₁₋₈alquilo)₂, CONHC₁₋₈alquilo, CON(C₁₋₈alquilo)₂, N(C₁₋₈alquilo)CONH(C₁₋₈alquilo), N(C₁₋₈alquilo)CON(C₁₋₈alquilo)₂, NHCONH(C₁₋₈alquilo), NHCON(C₁₋₈alquilo)₂, NHCONH₂, N(C₁₋₈alquilo)SO₂NH(C₁₋₈alquilo), N(C₁₋₈alquilo)SO₂N(C₁₋₈alquilo)₂, NH SO₂NH(C₁₋₈alquilo), NH SO₂N(C₁₋₈alquilo)₂ o NH SO₂NH₂.

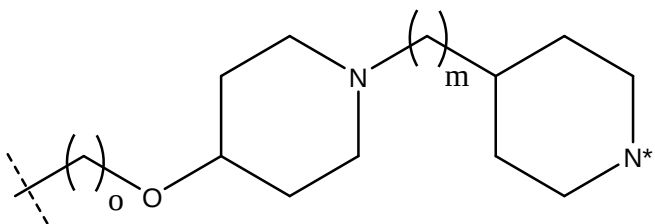
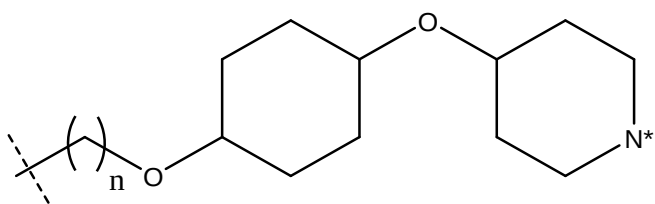
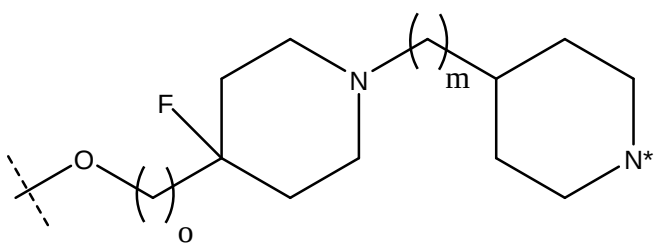
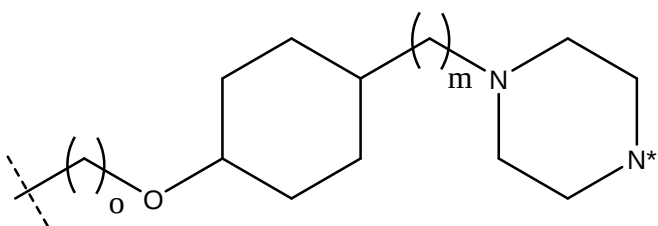
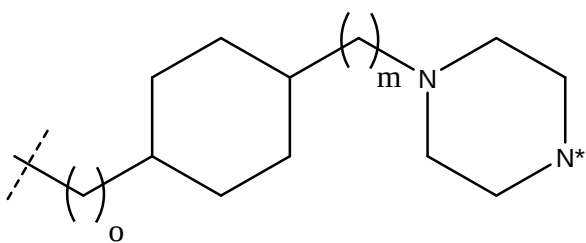
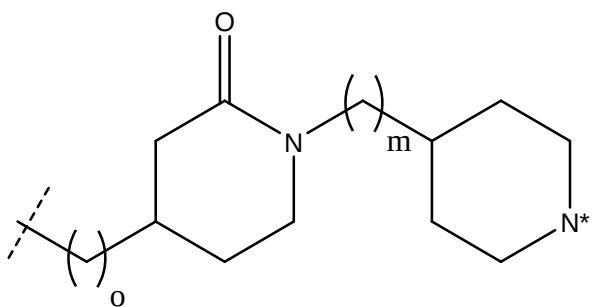
19. El compuesto de cualquiera de las reivindicaciones 1-18, en donde L se selecciona del grupo que consiste en:

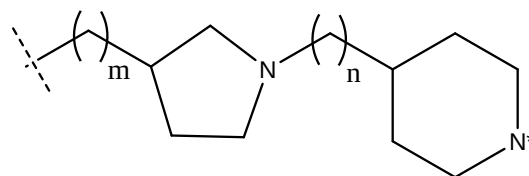
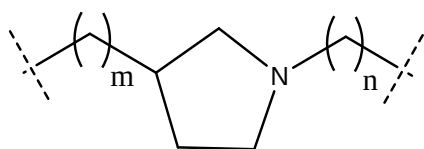
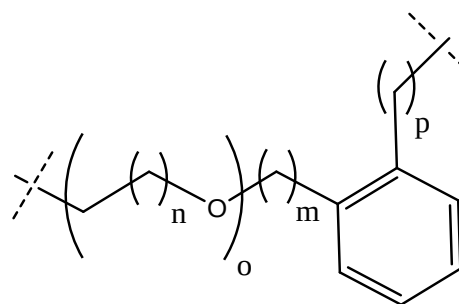
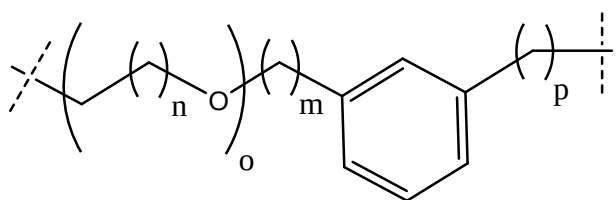
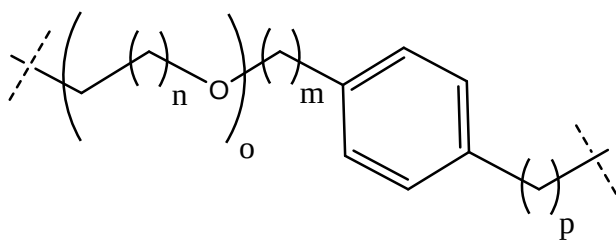
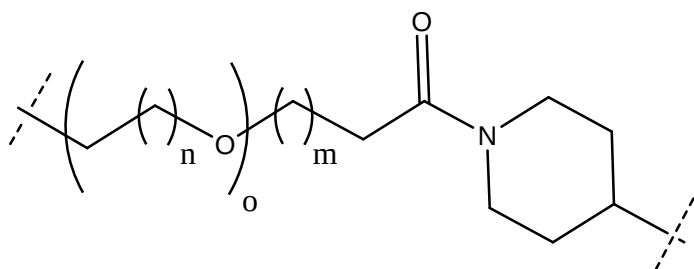
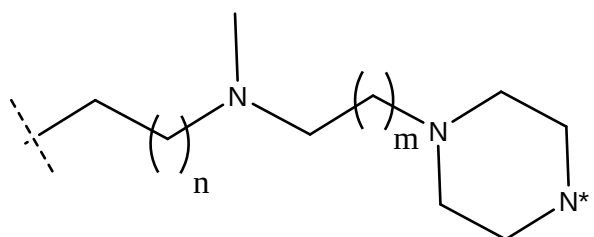
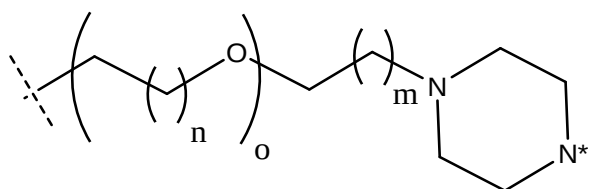
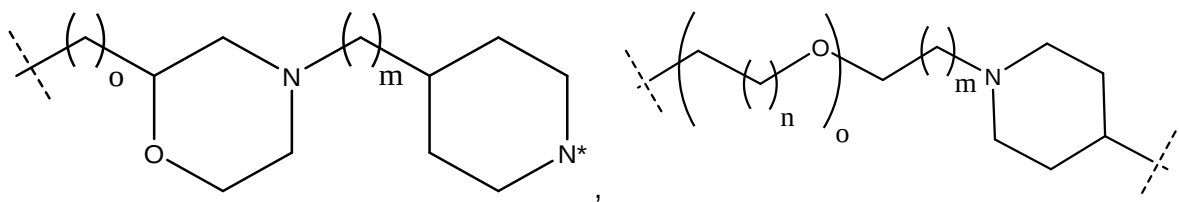


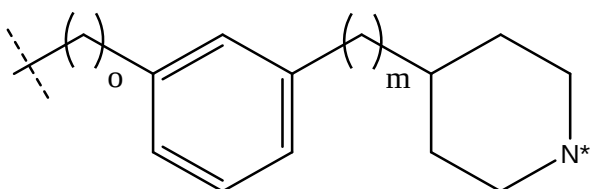
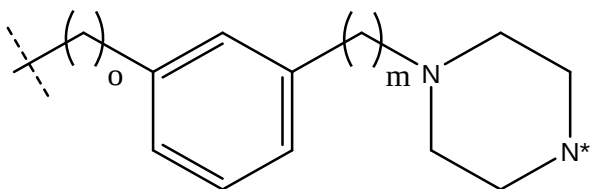
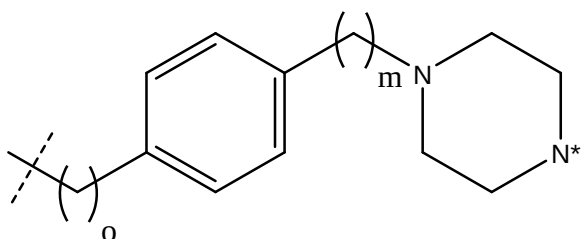
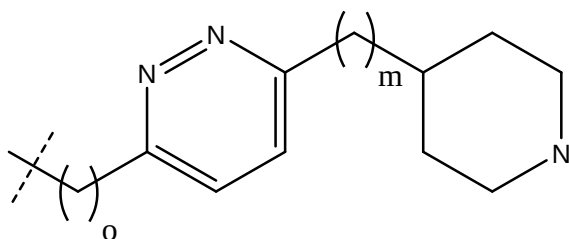
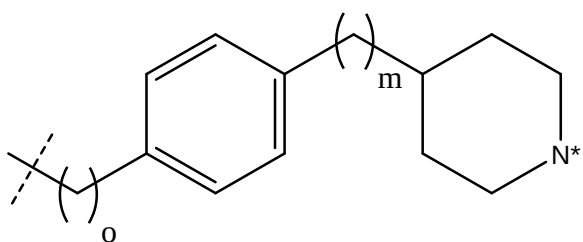
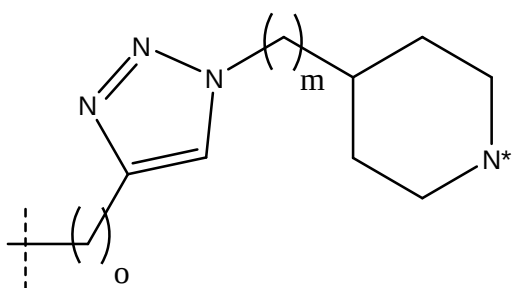
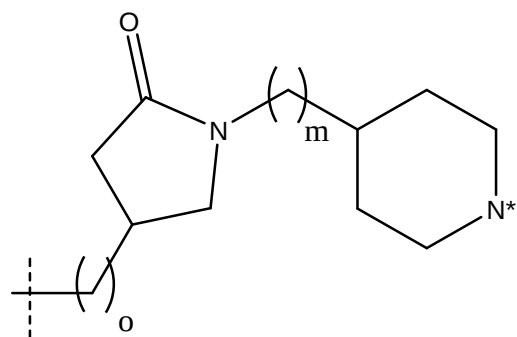
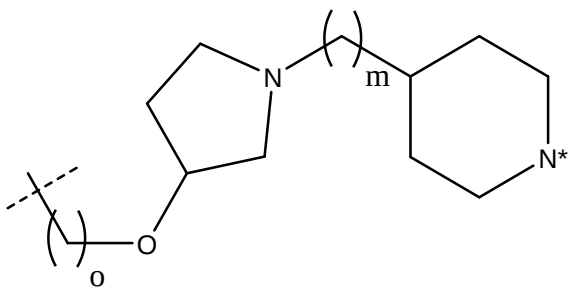
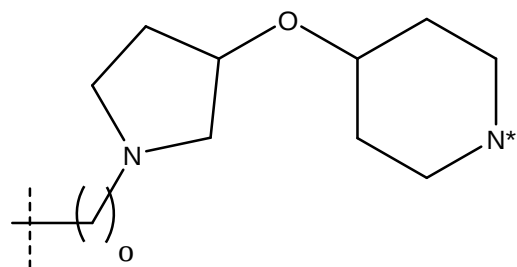
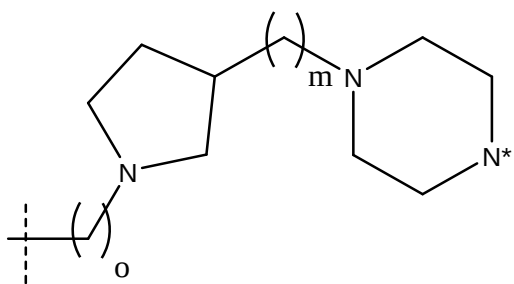


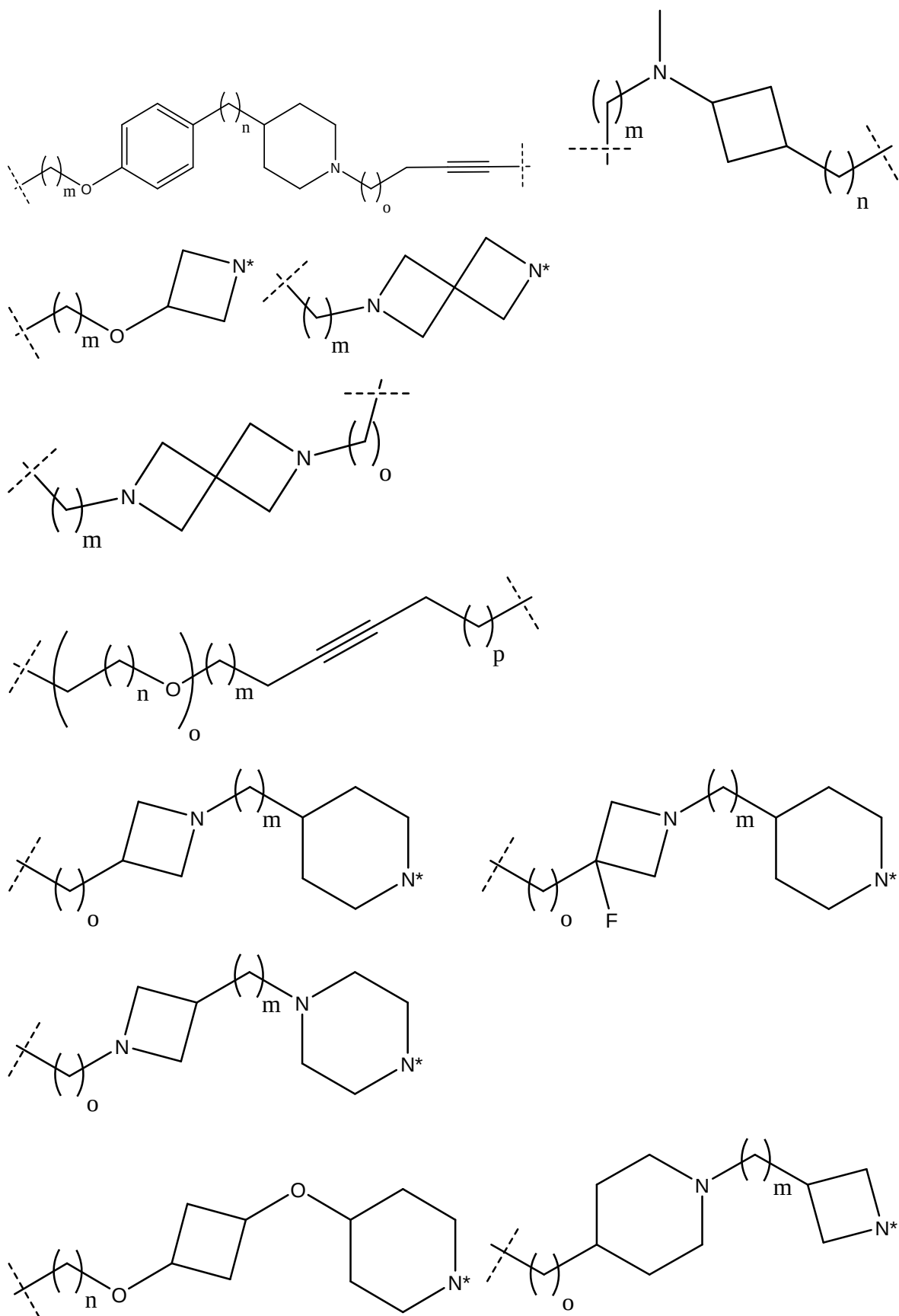


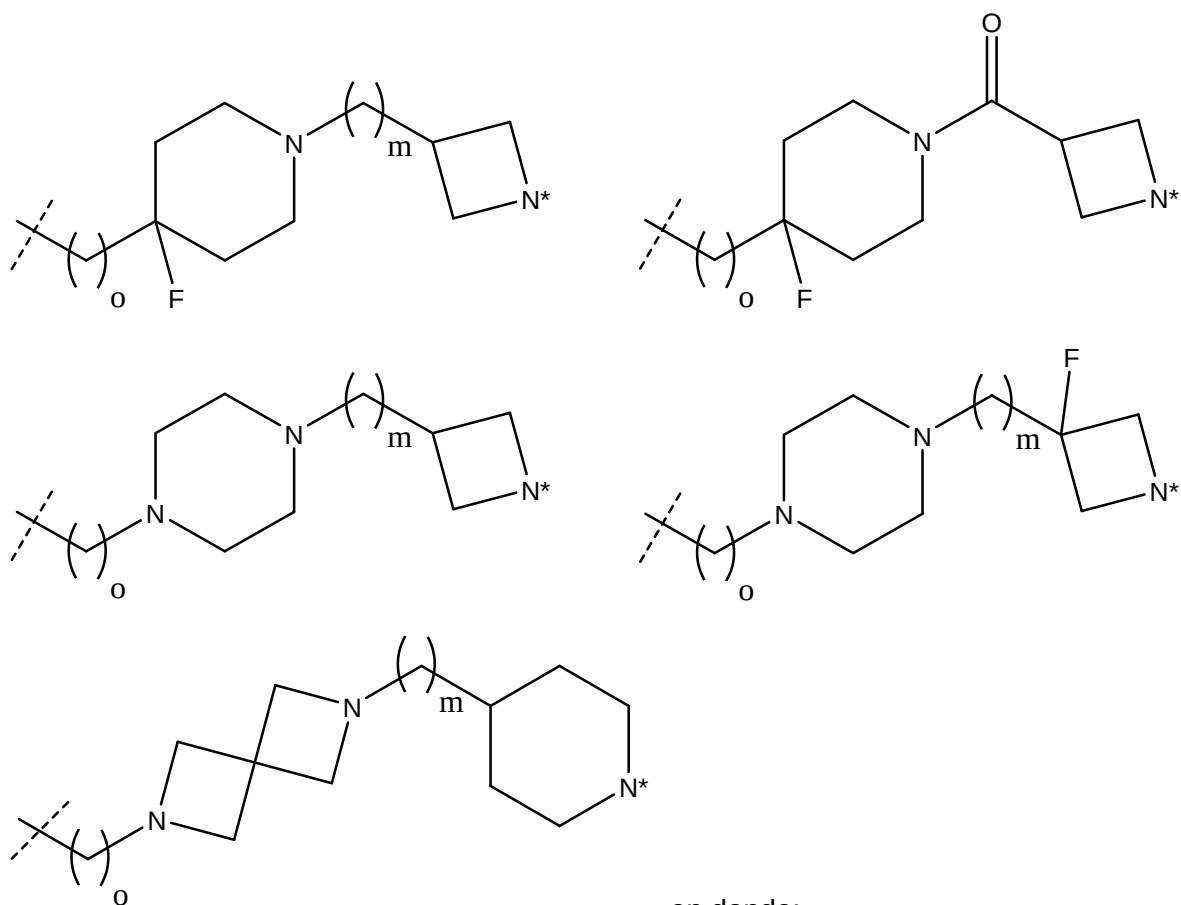












, en donde:

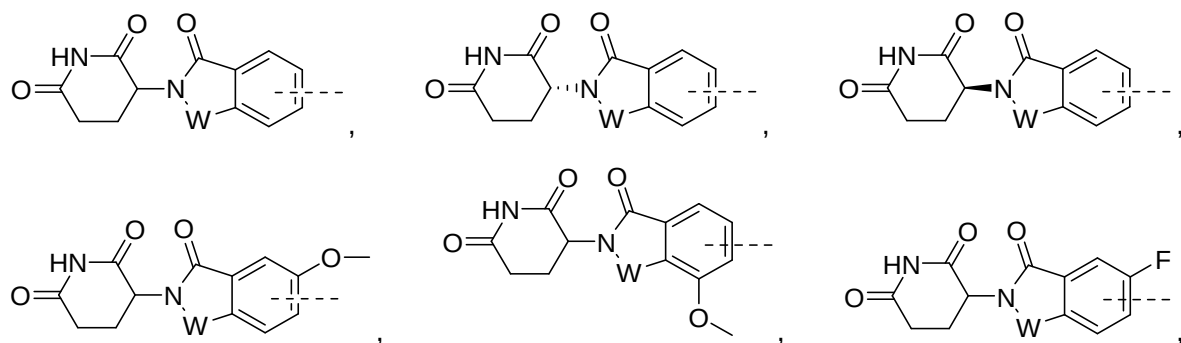
el grupo enlazador químico se sustituye opcionalmente con un halógeno;

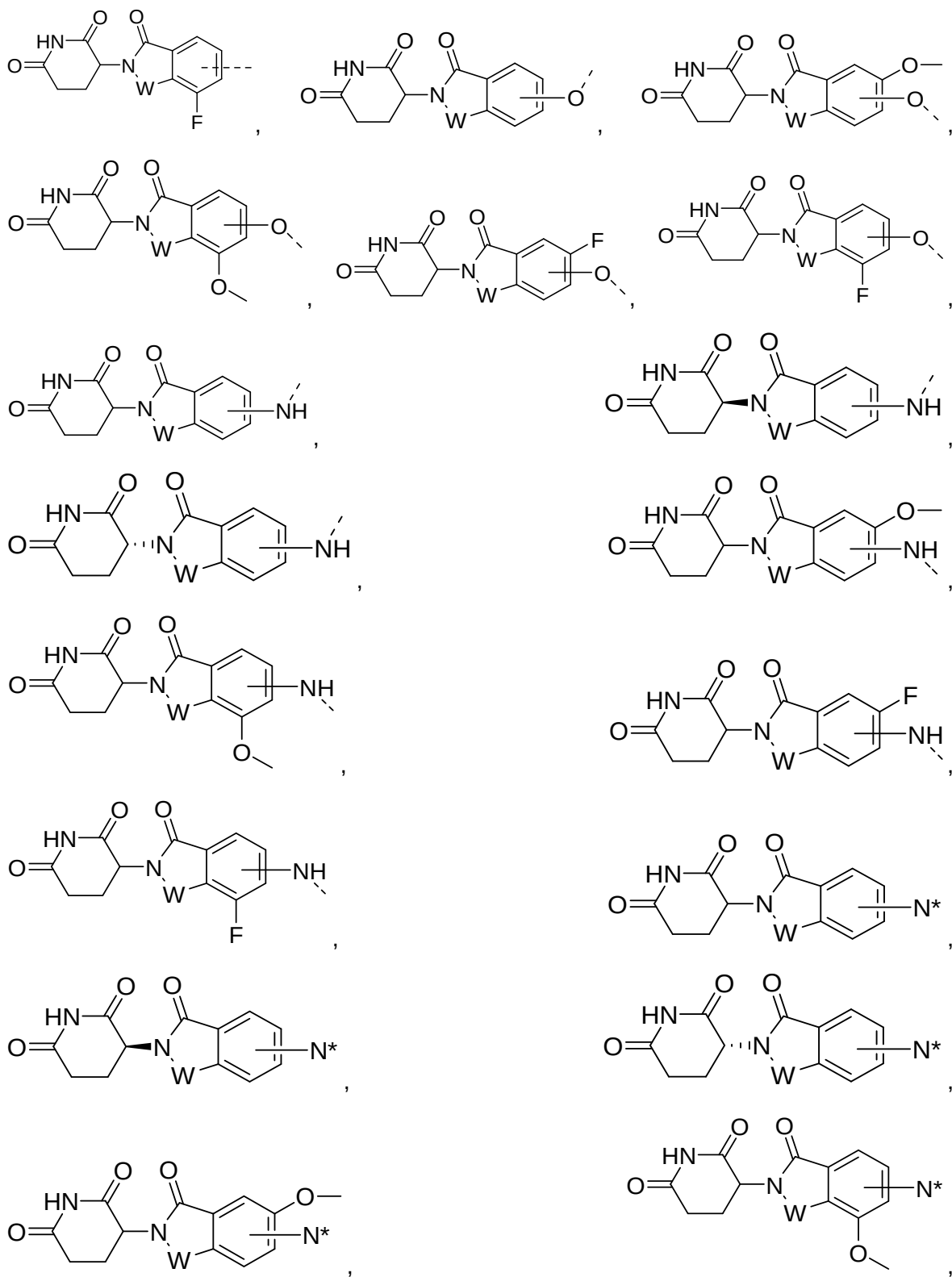
N* es un átomo de nitrógeno que está unido covalentemente o compartido con el CLM o el PTM; y

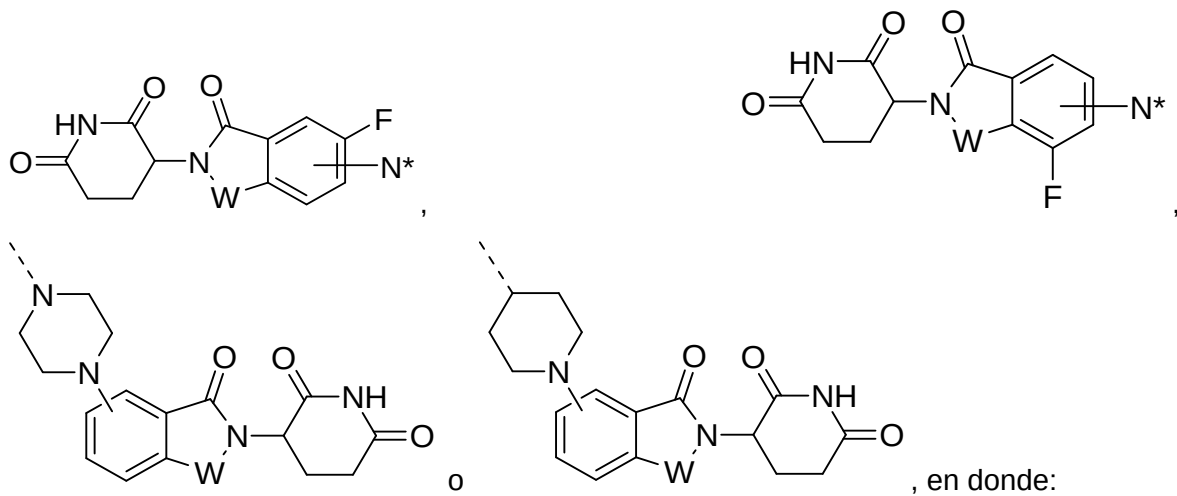
cada m, n, o, p, q y r de L es independientemente 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 o 20.

20. El compuesto de cualquiera de las reivindicaciones 1-19, en donde al menos uno de:

(a) el CLM está representado por:



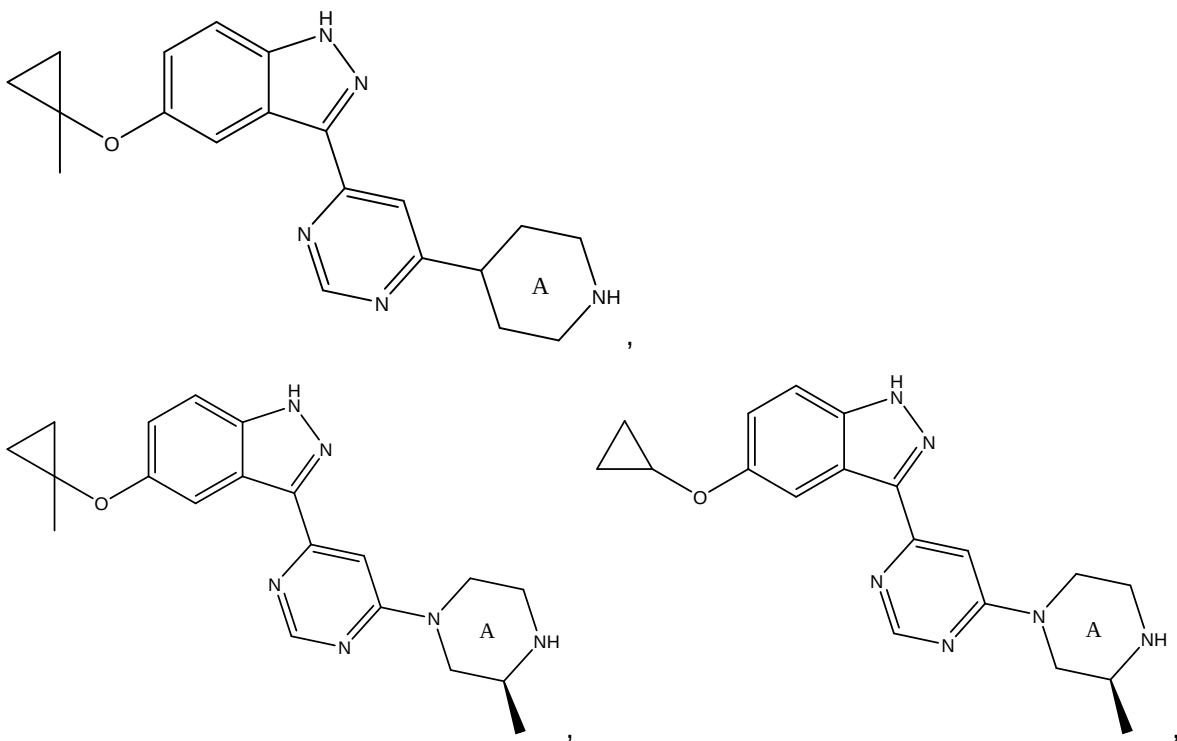


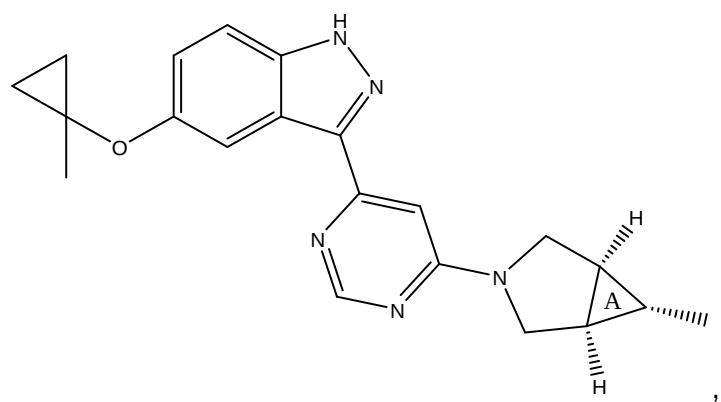
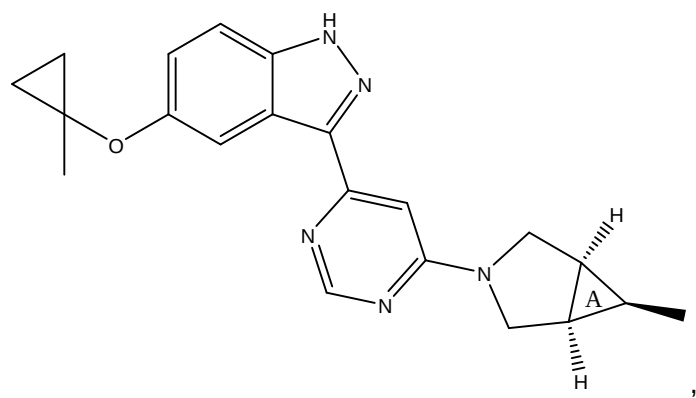
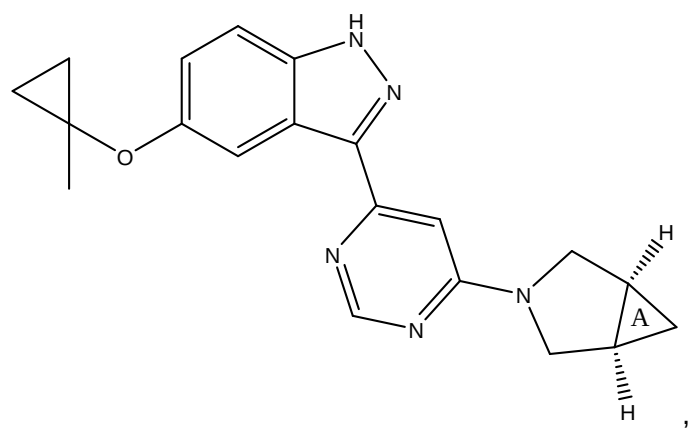
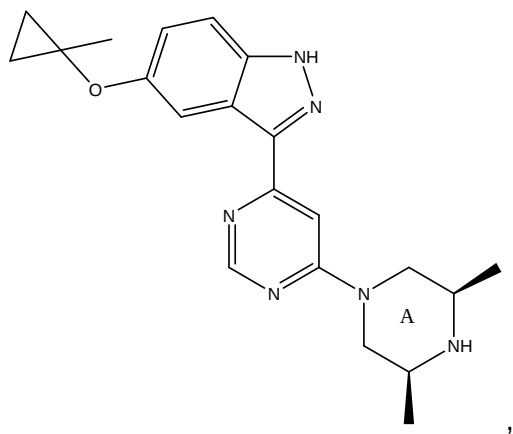


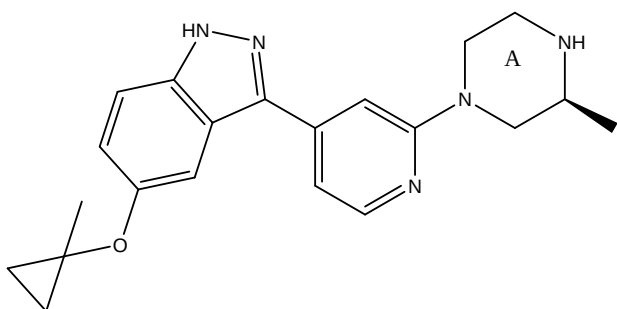
--- del ULM indica el punto de unión con la L; y

N* es un átomo de nitrógeno que se comparte con L;

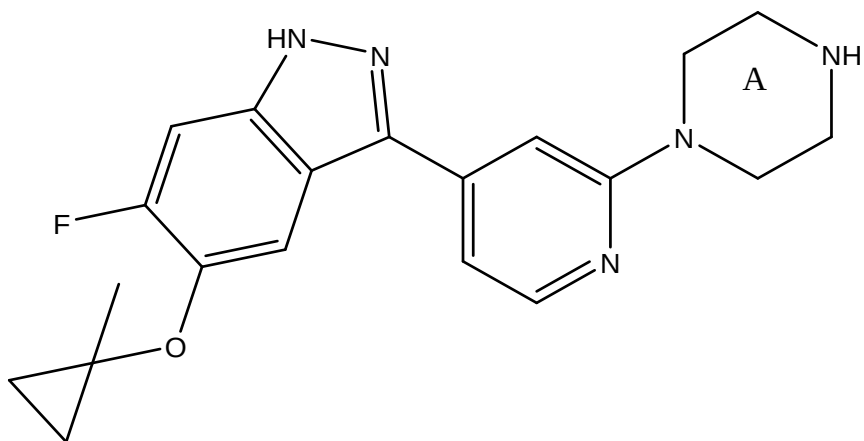
(b) el PTM está representado por:



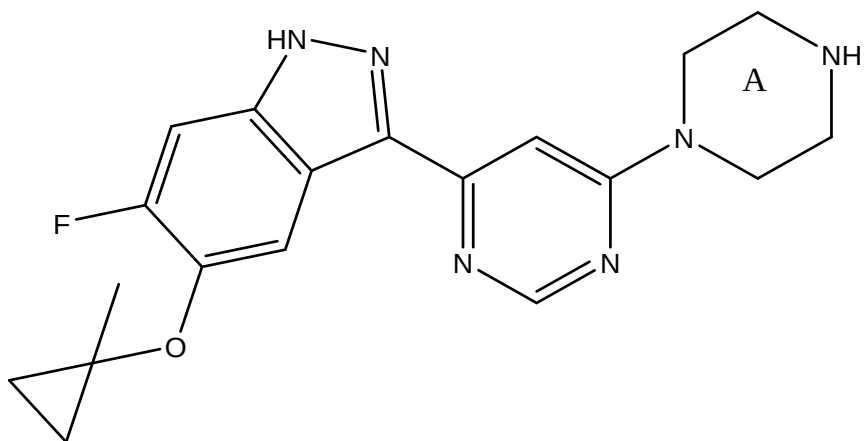




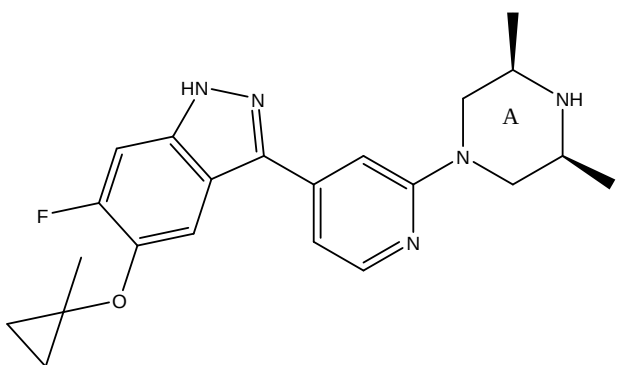
,



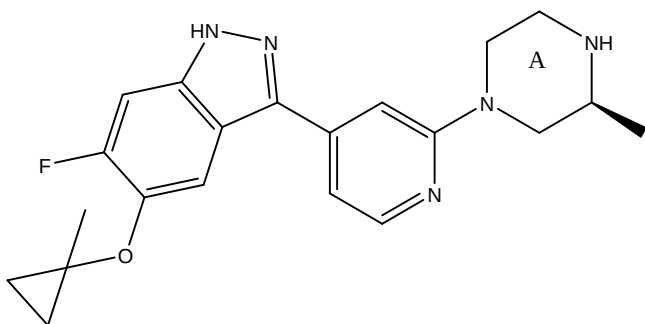
,



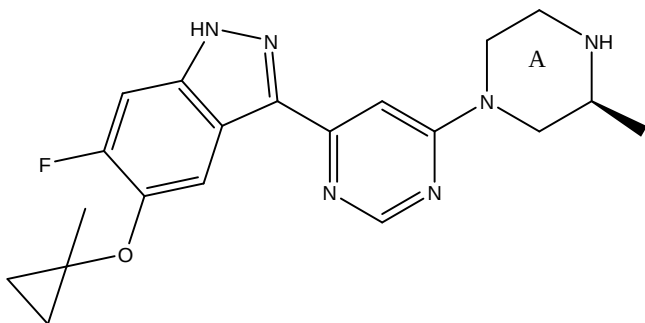
,



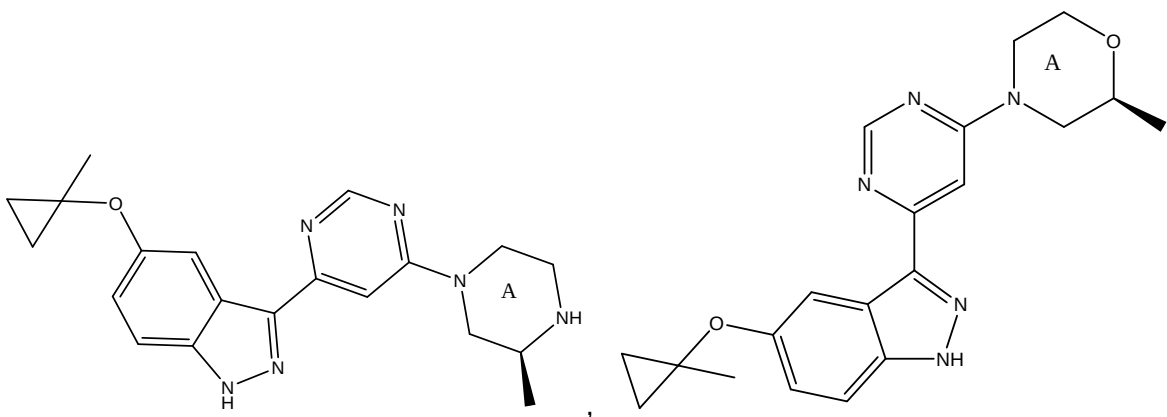
,



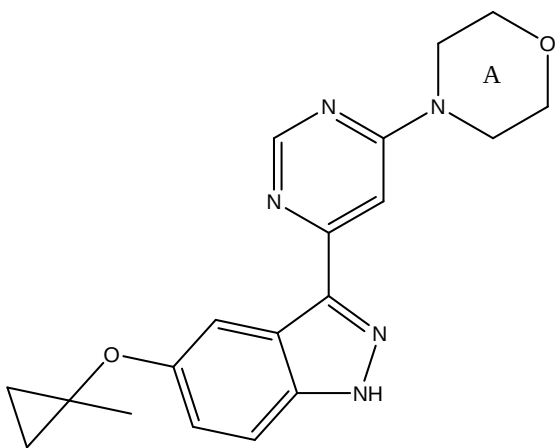
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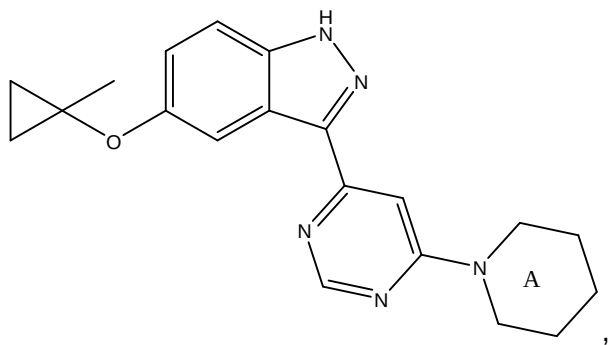
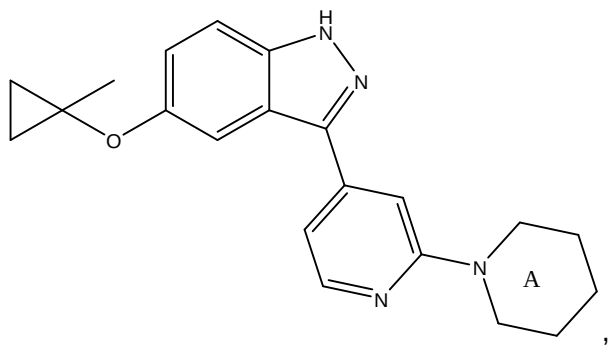
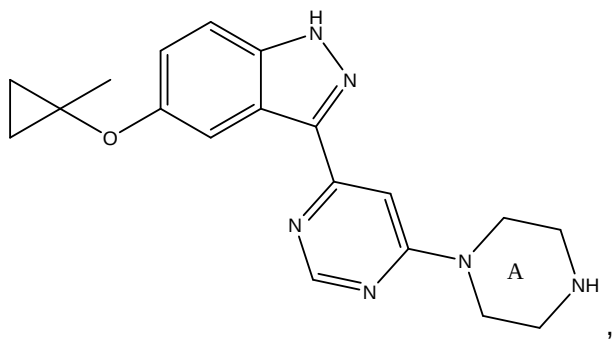
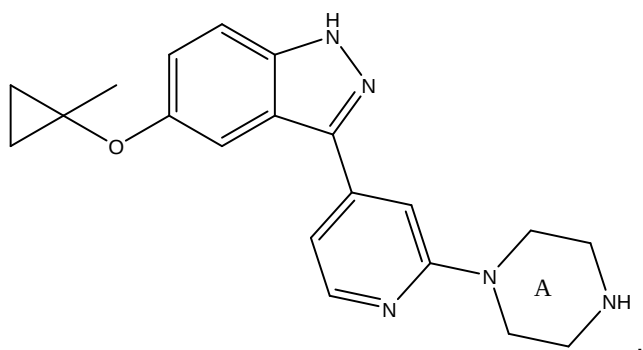
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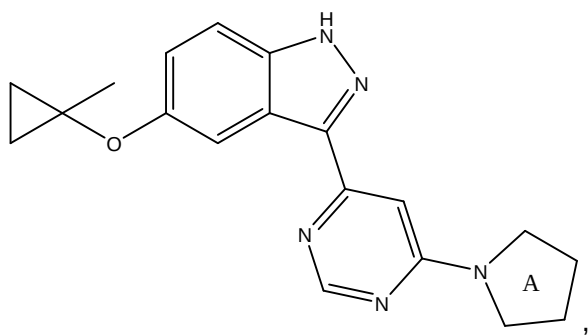
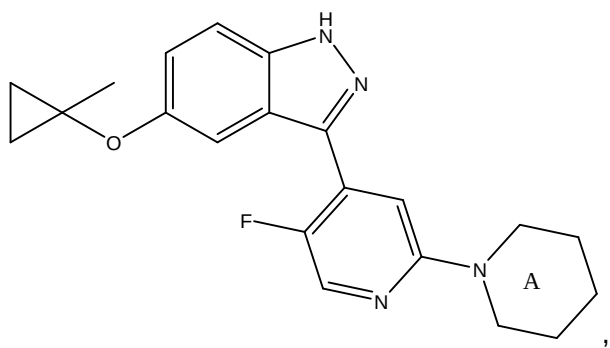
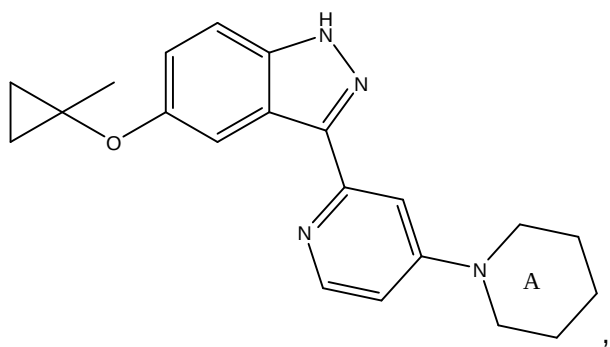
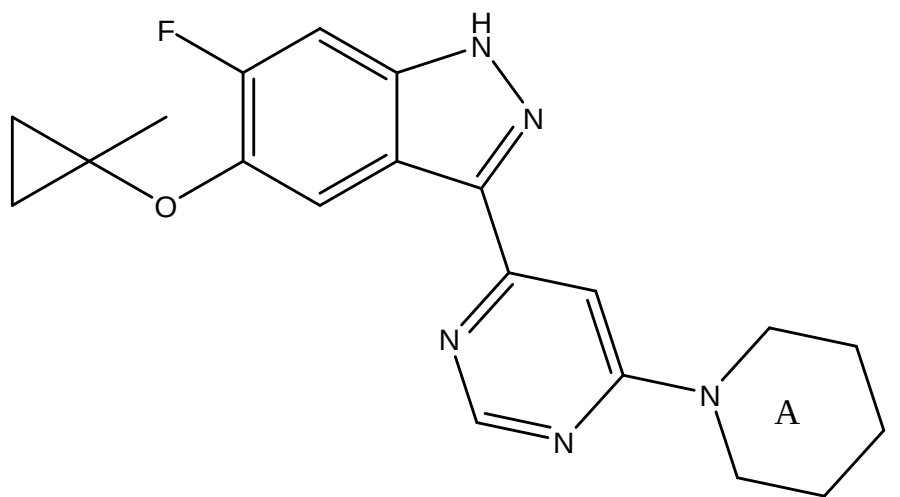


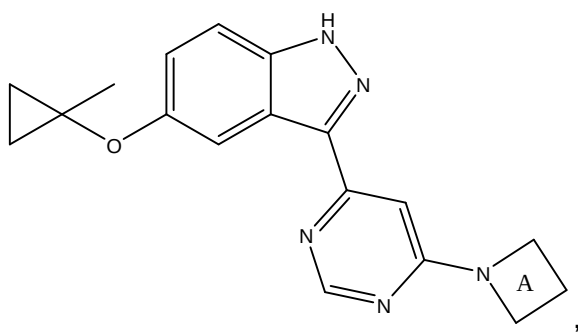
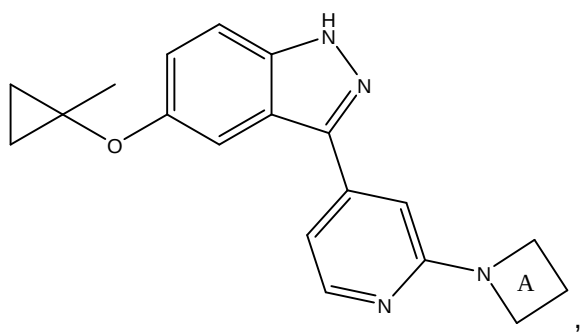
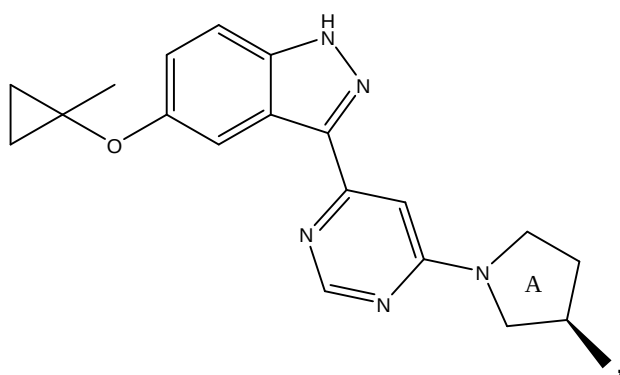
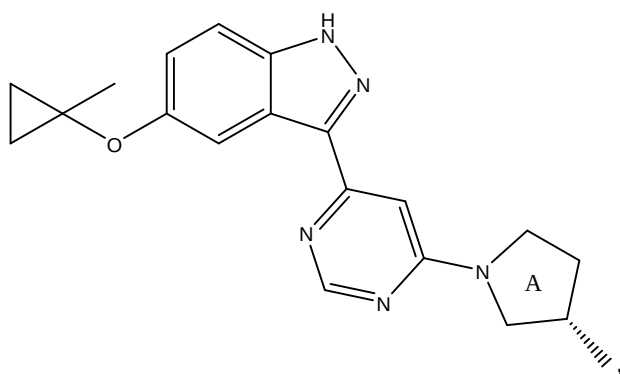
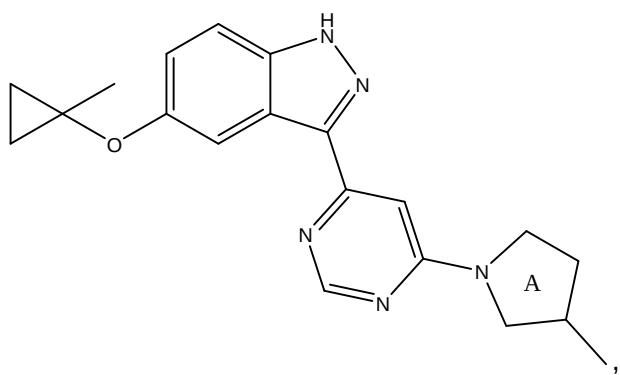
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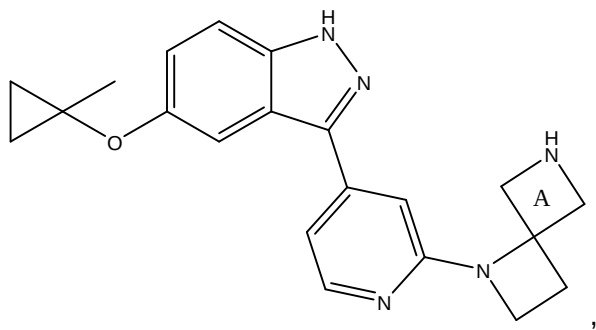
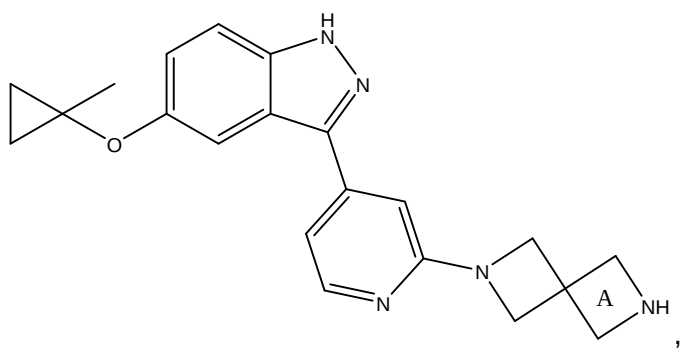
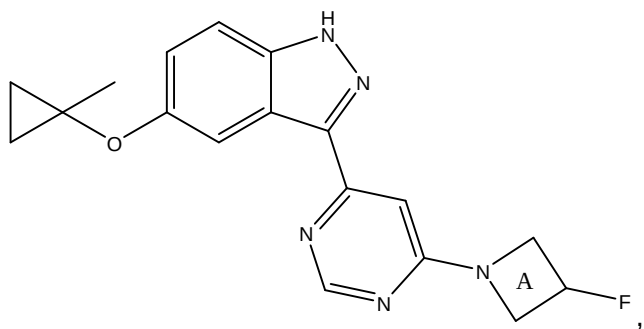
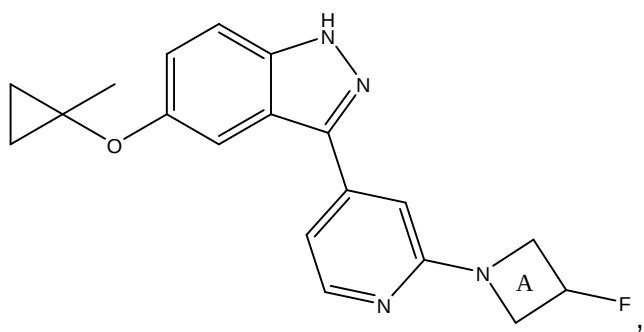


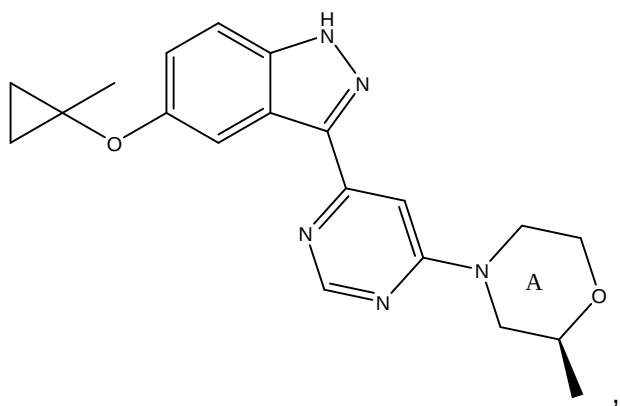
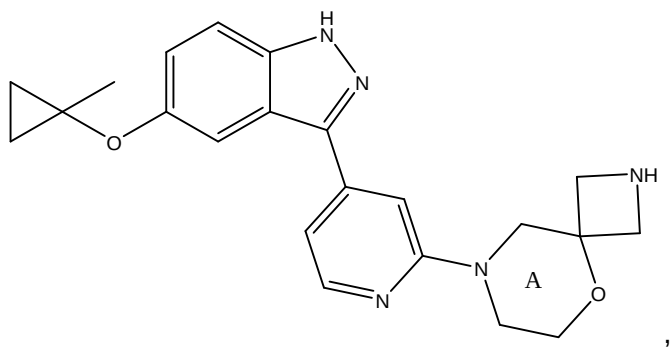
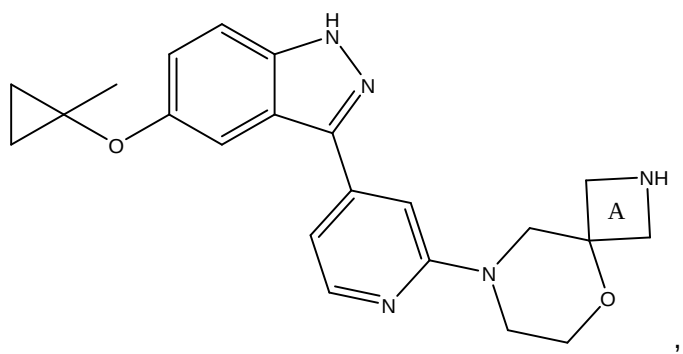
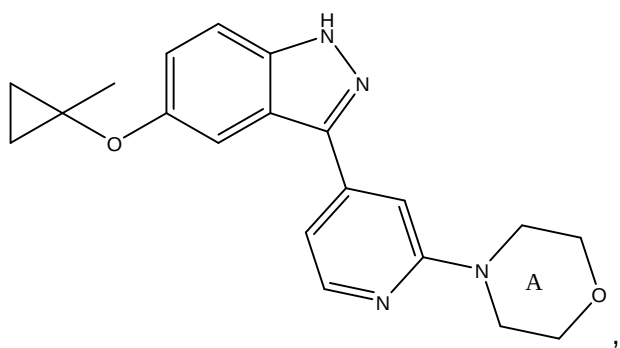
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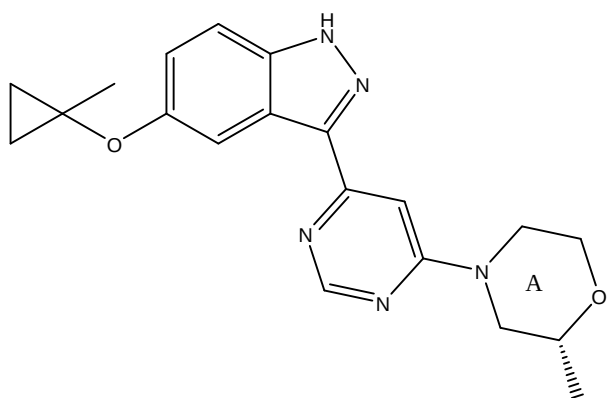




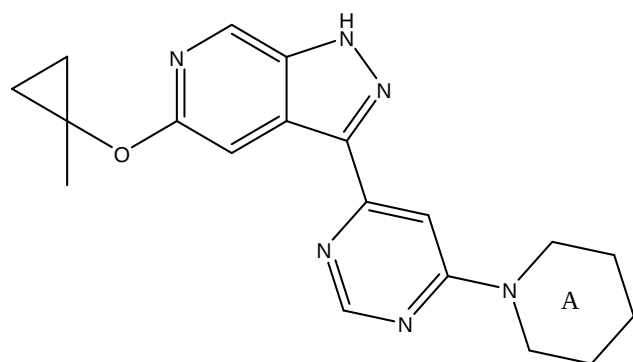






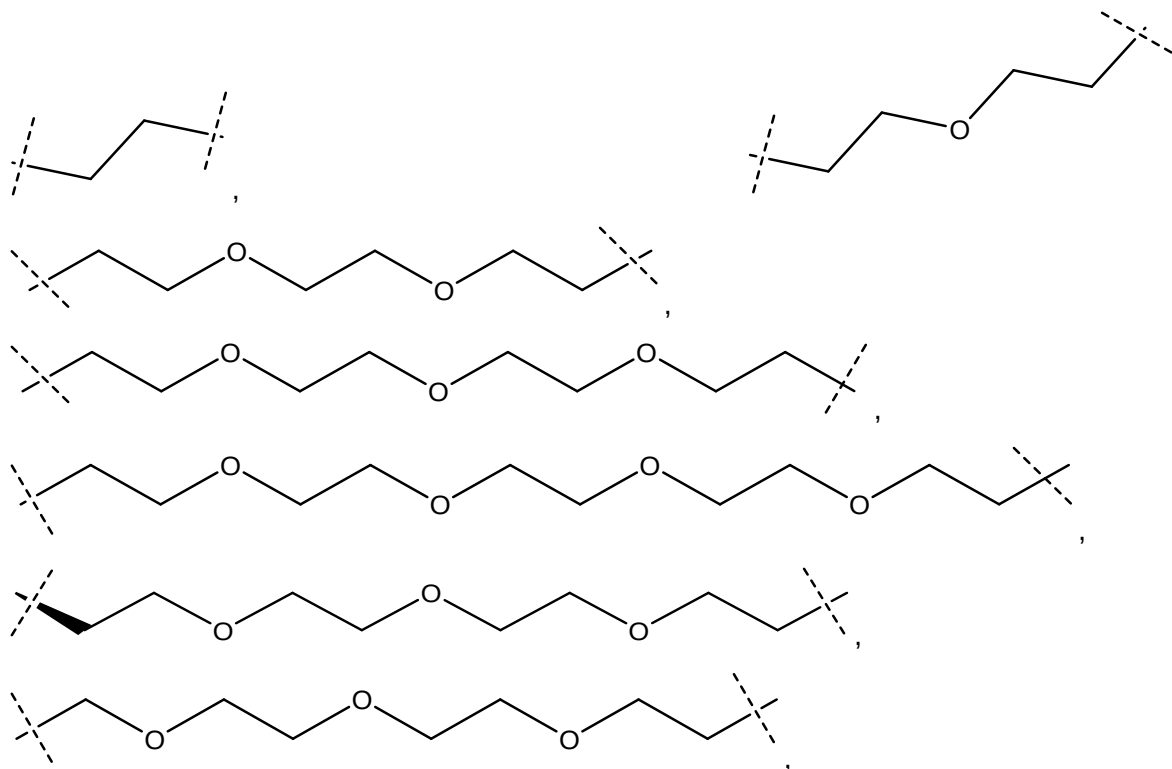


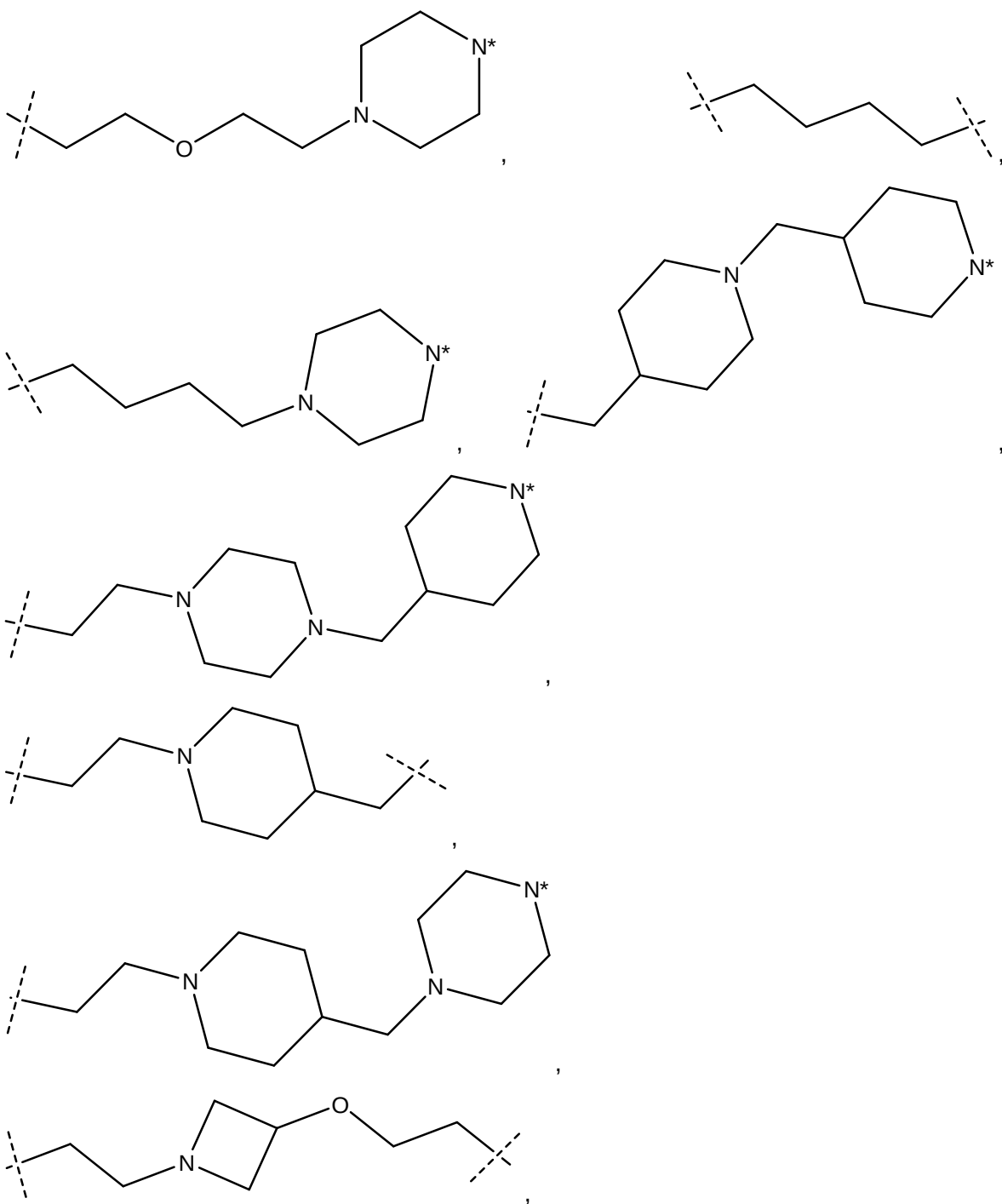
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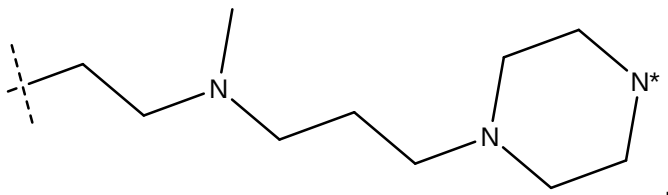
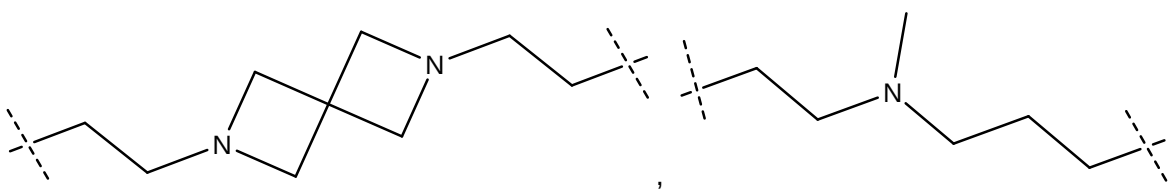
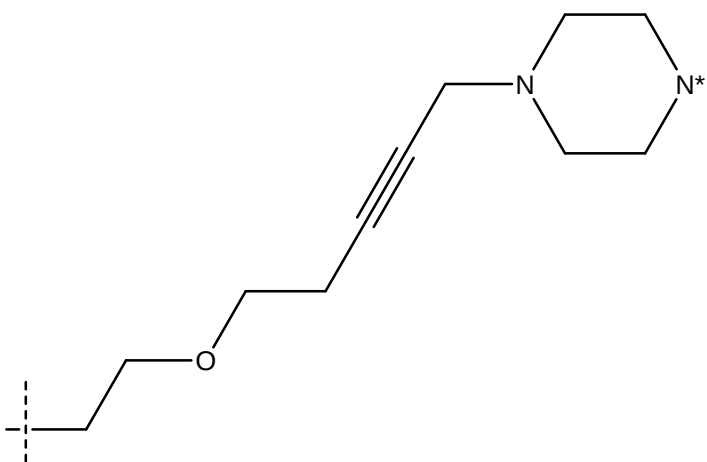
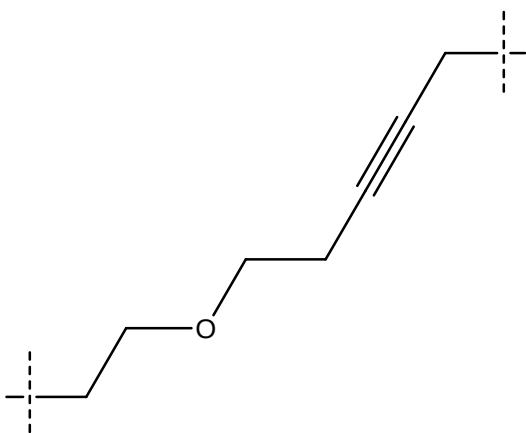


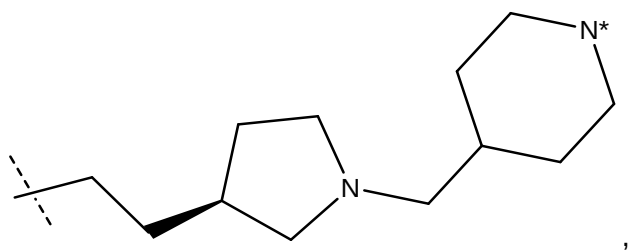
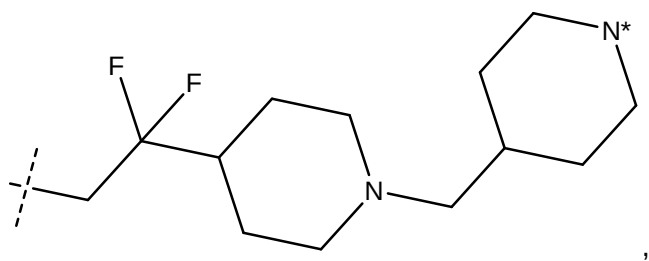
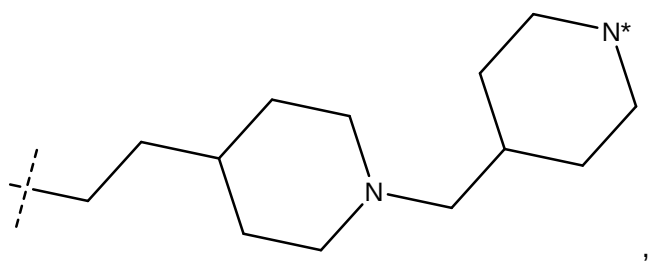
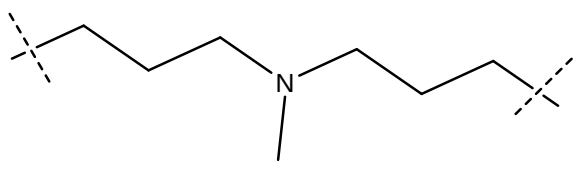
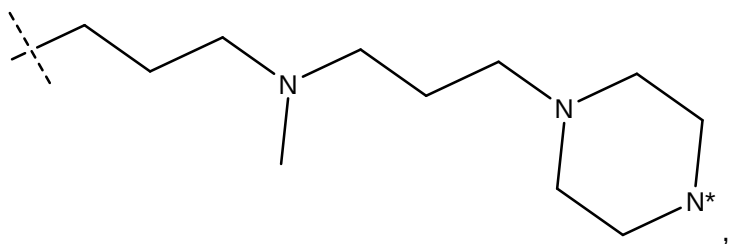
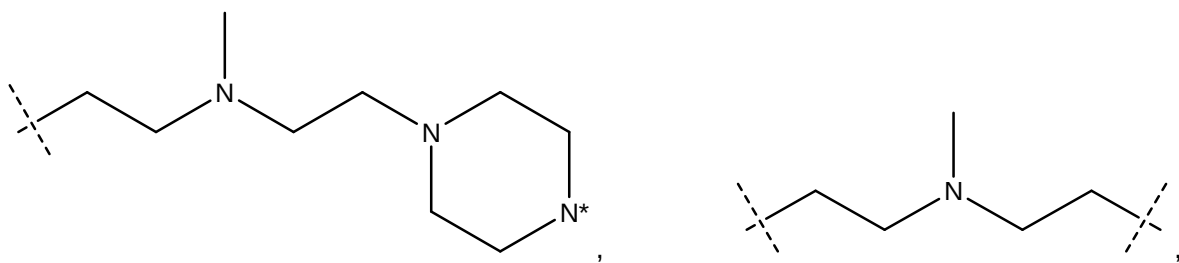
, en donde la PTM está unida covalentemente a la L a través de un átomo de heterocicloalquilo A o un sustituyente de este;

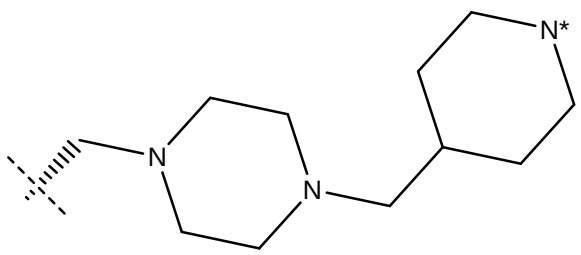
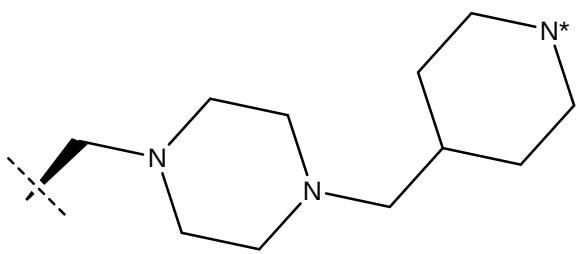
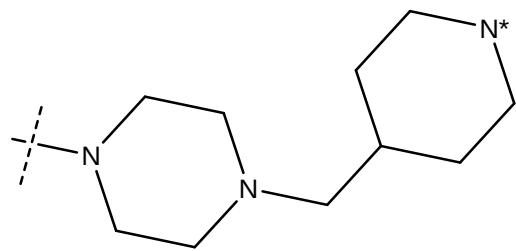
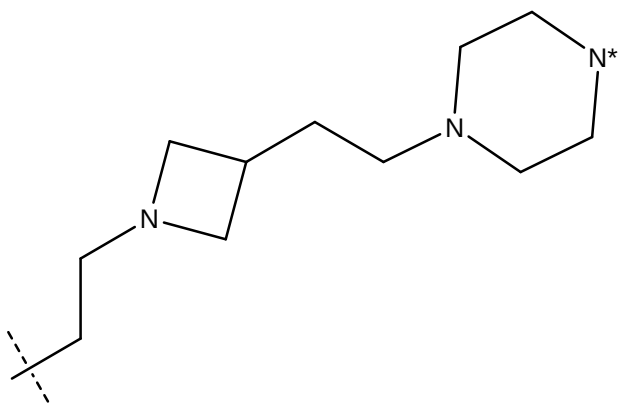
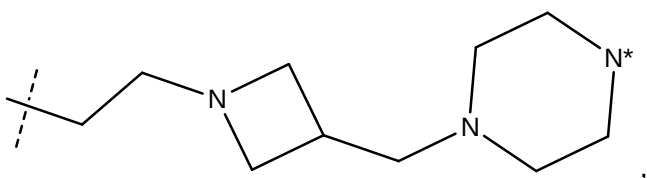
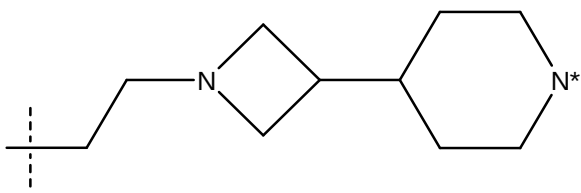
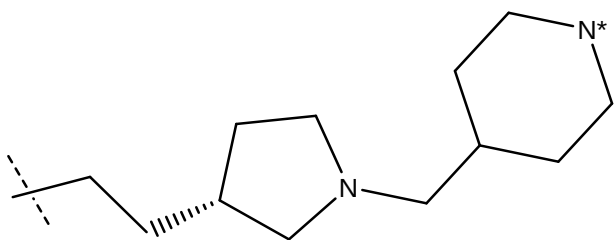
(c) L es un grupo enlazador (L) que se selecciona de:

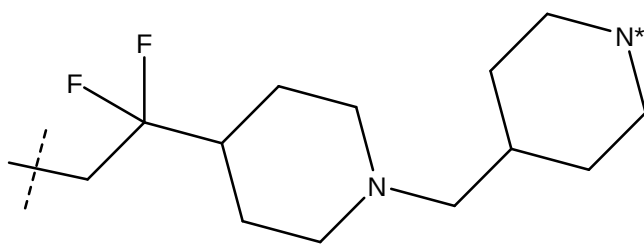
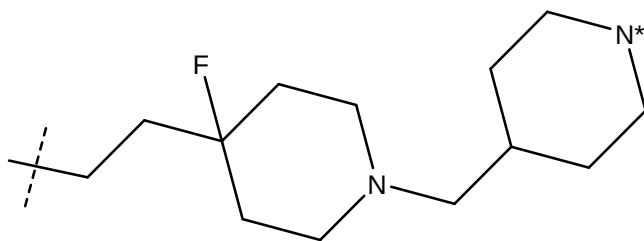
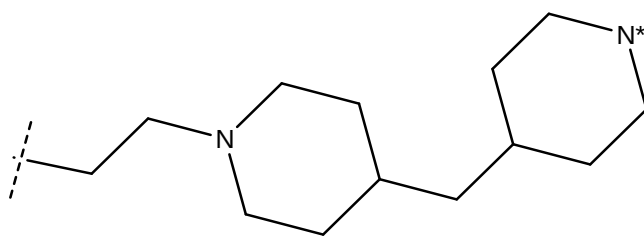
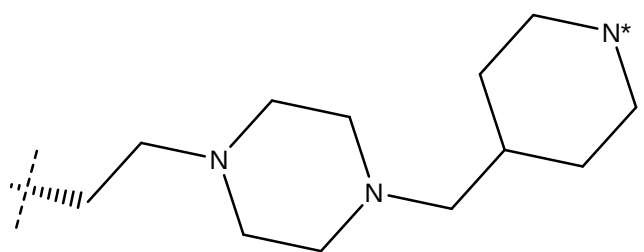
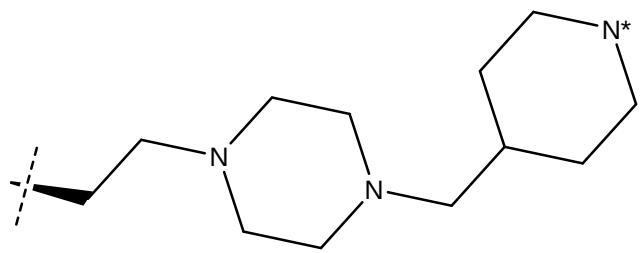
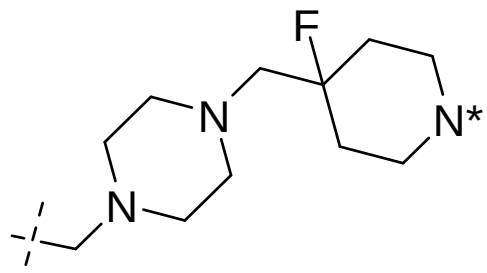
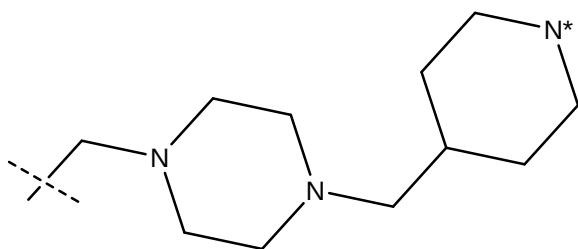


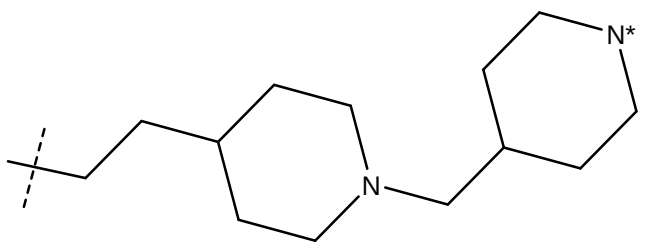




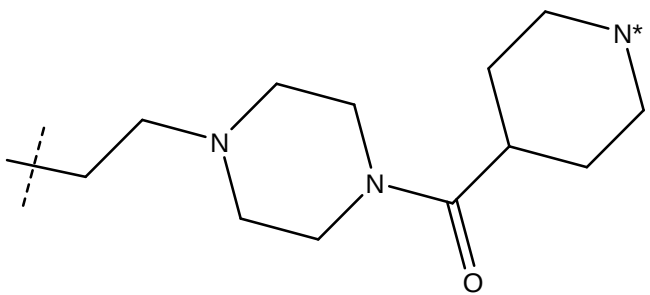




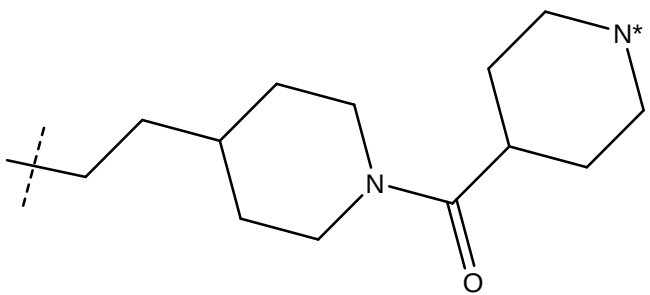




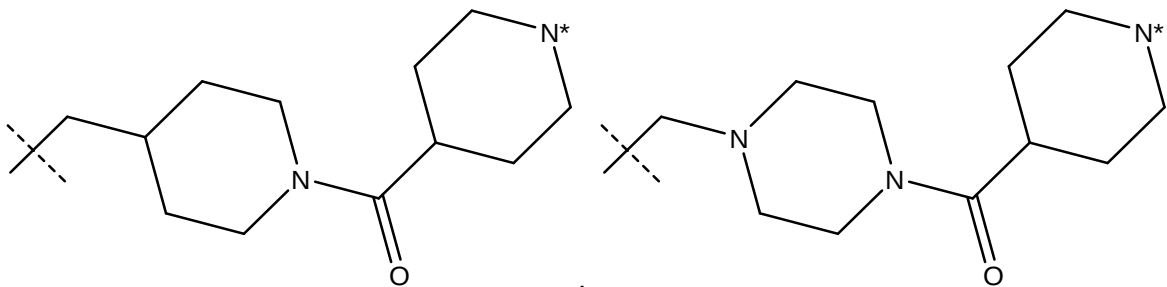
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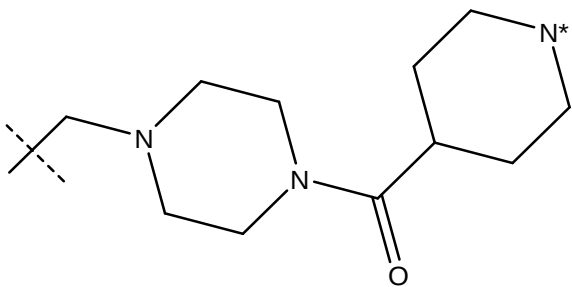
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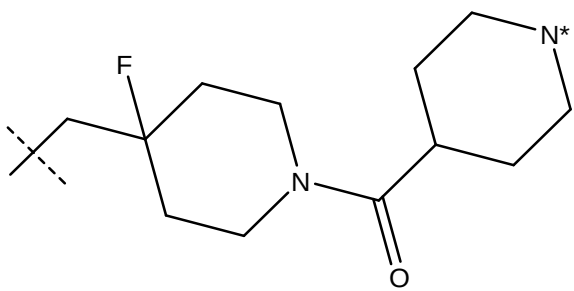
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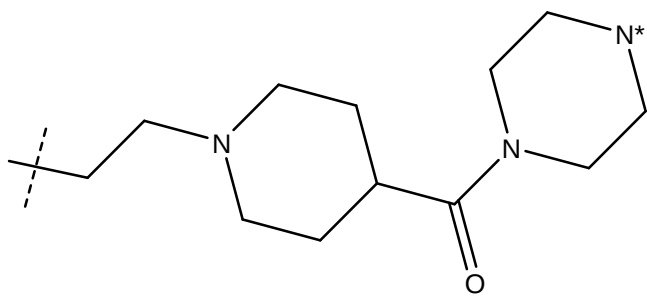
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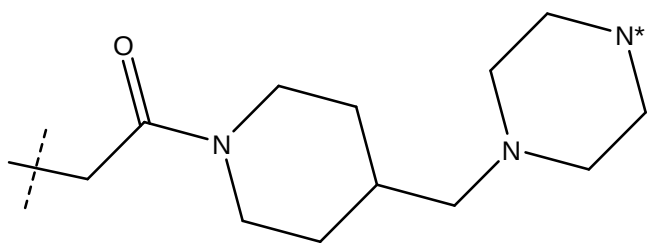
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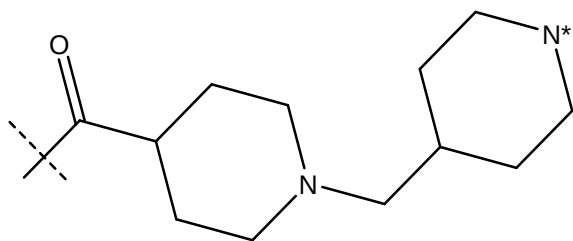
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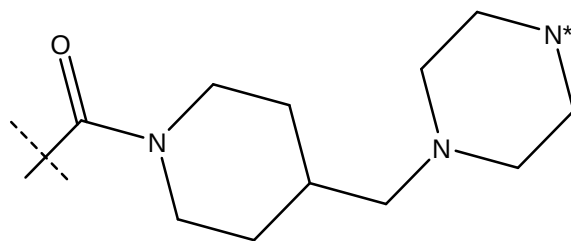
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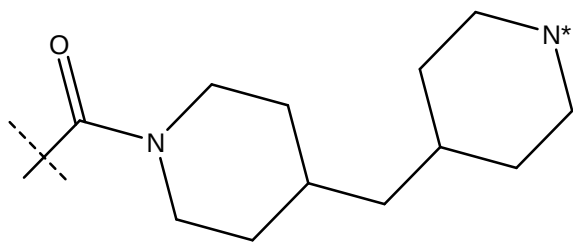
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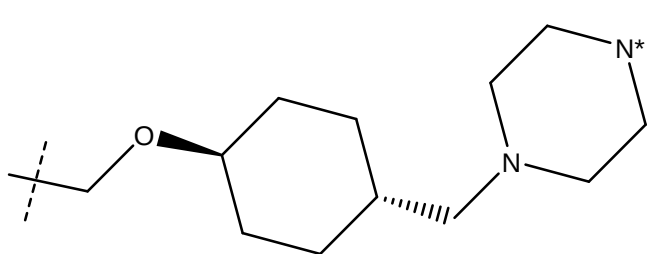
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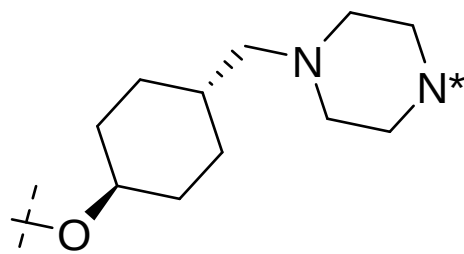
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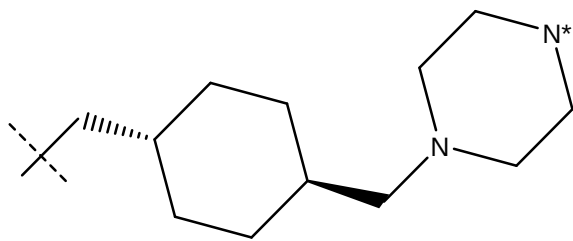
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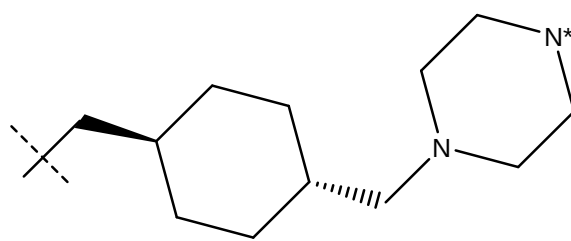
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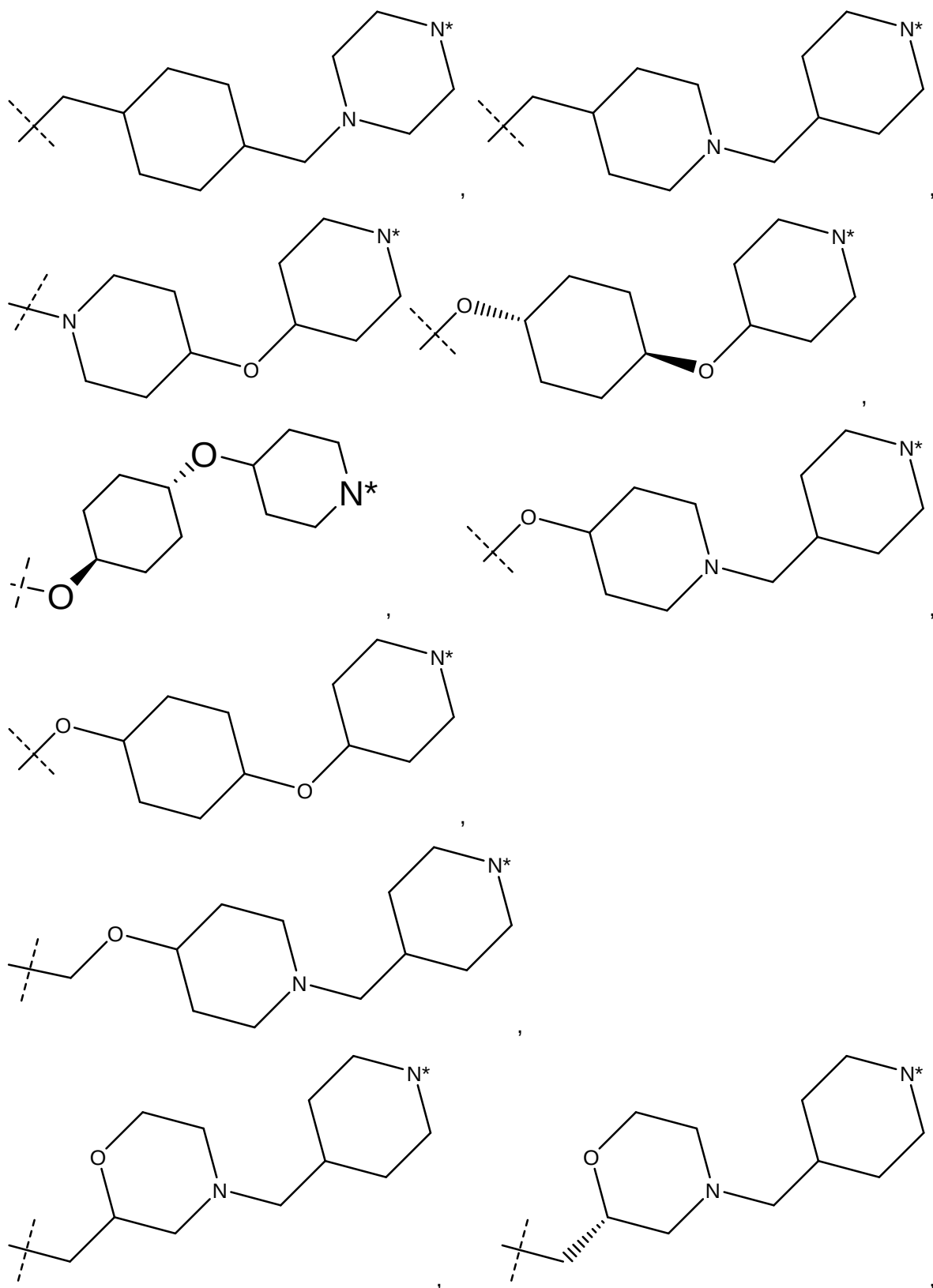
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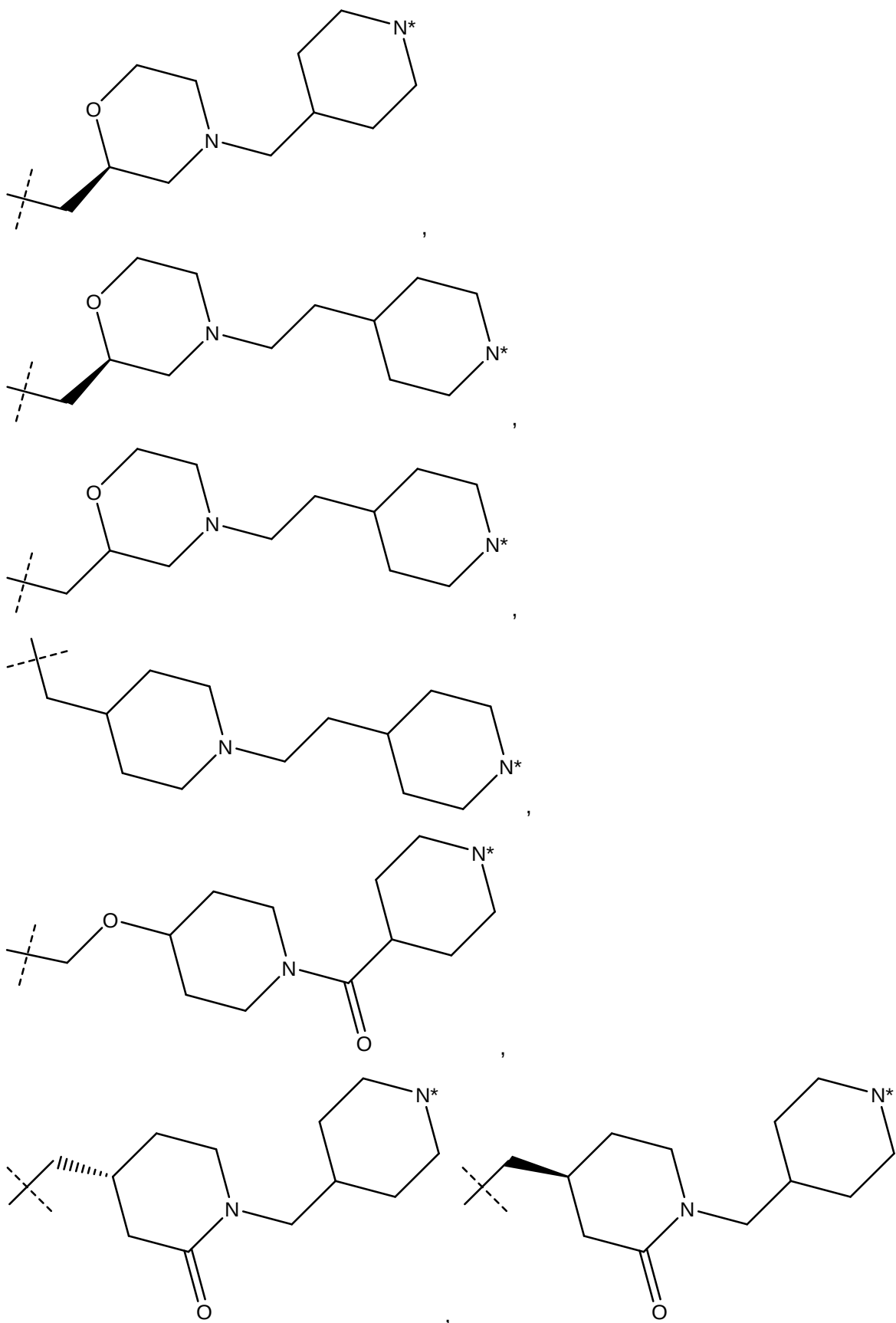


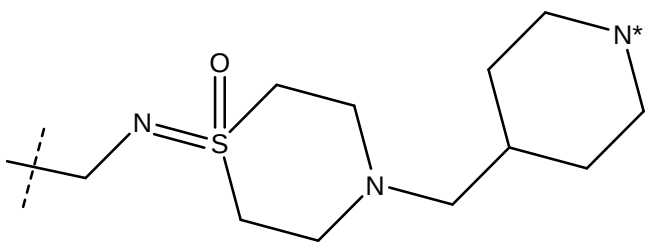
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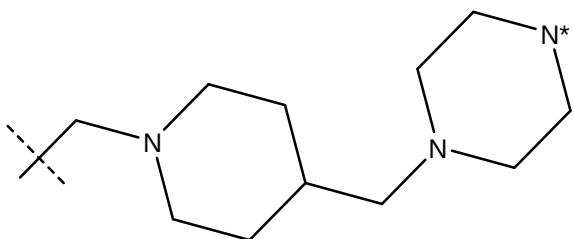
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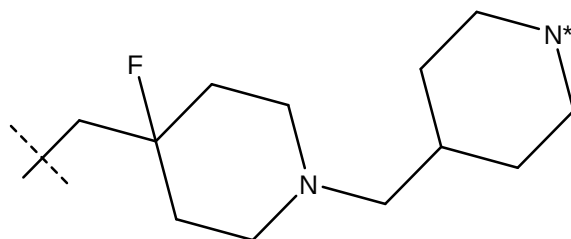




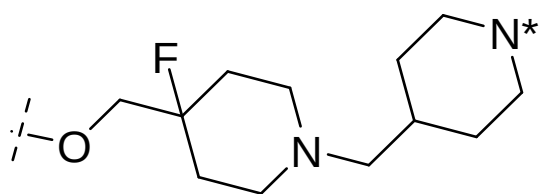
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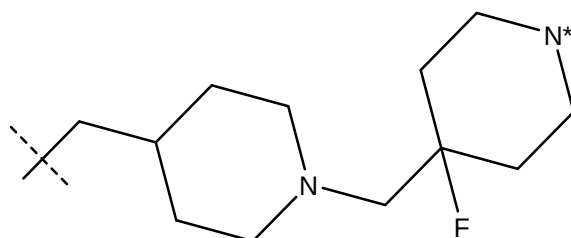
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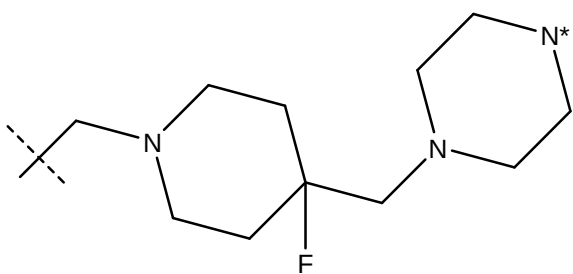
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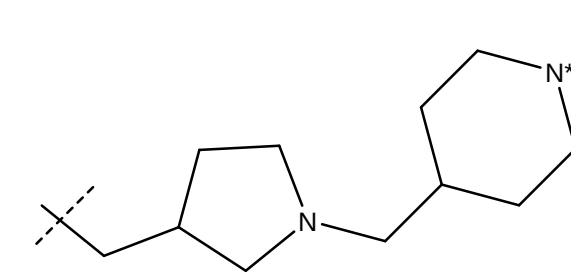
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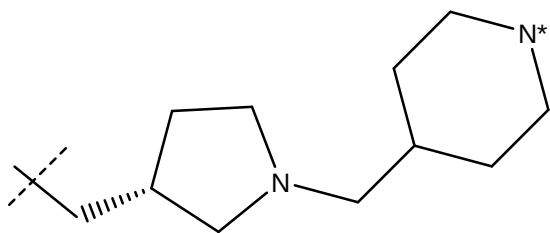
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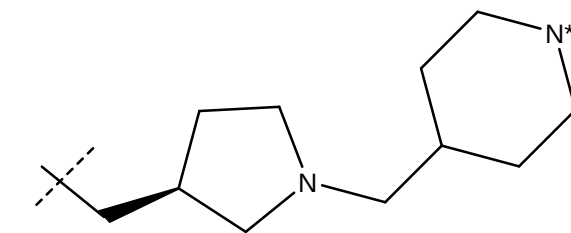
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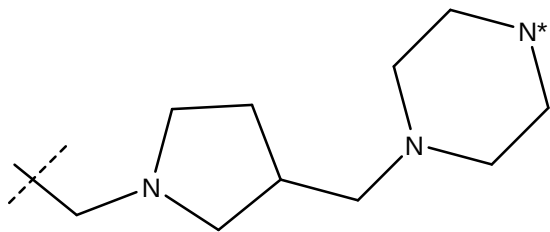
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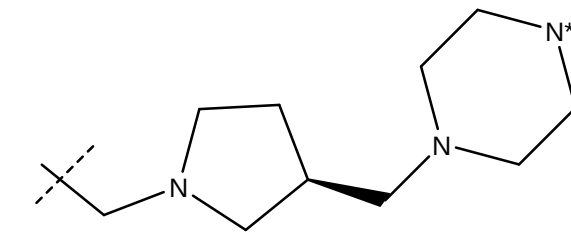
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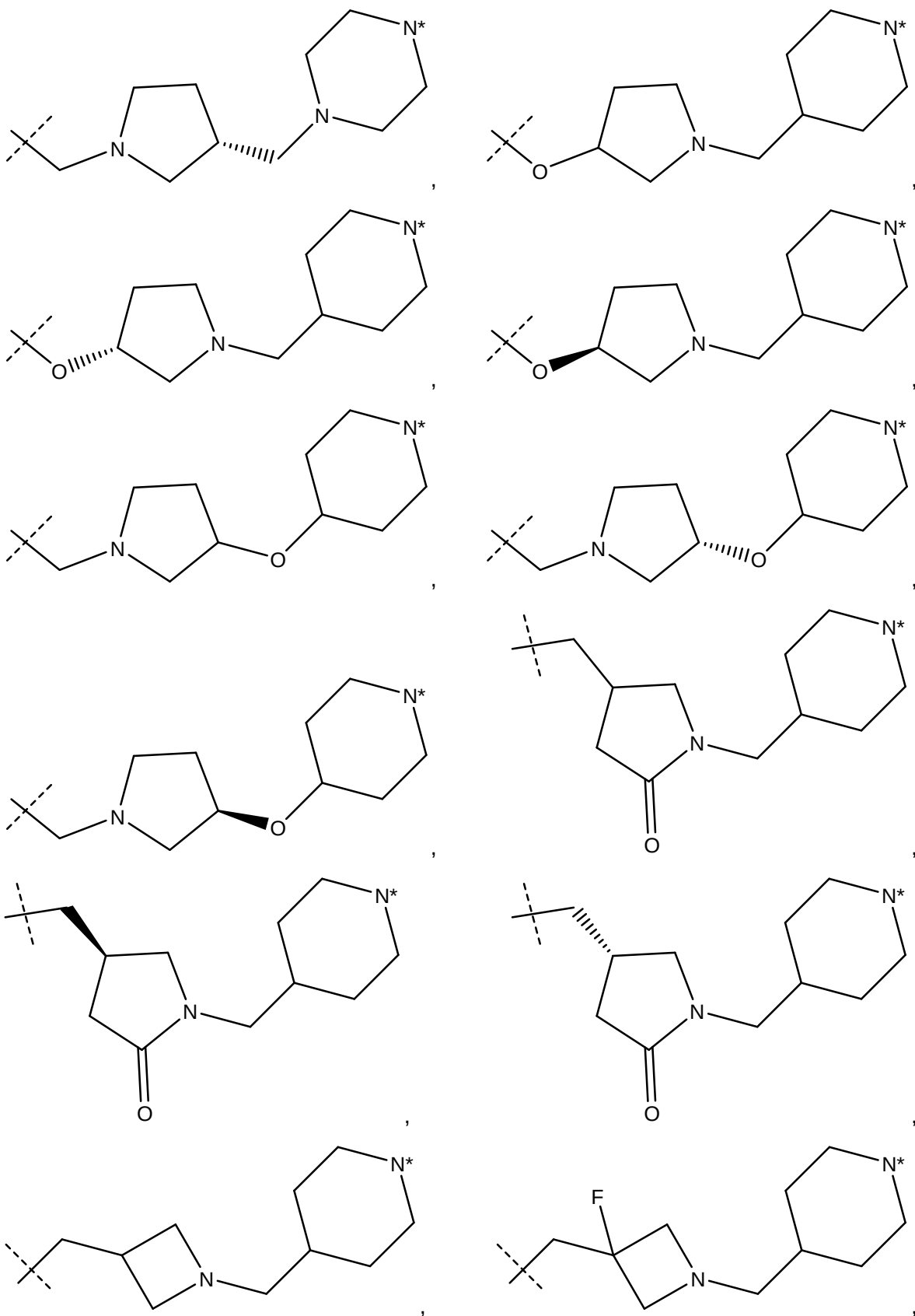
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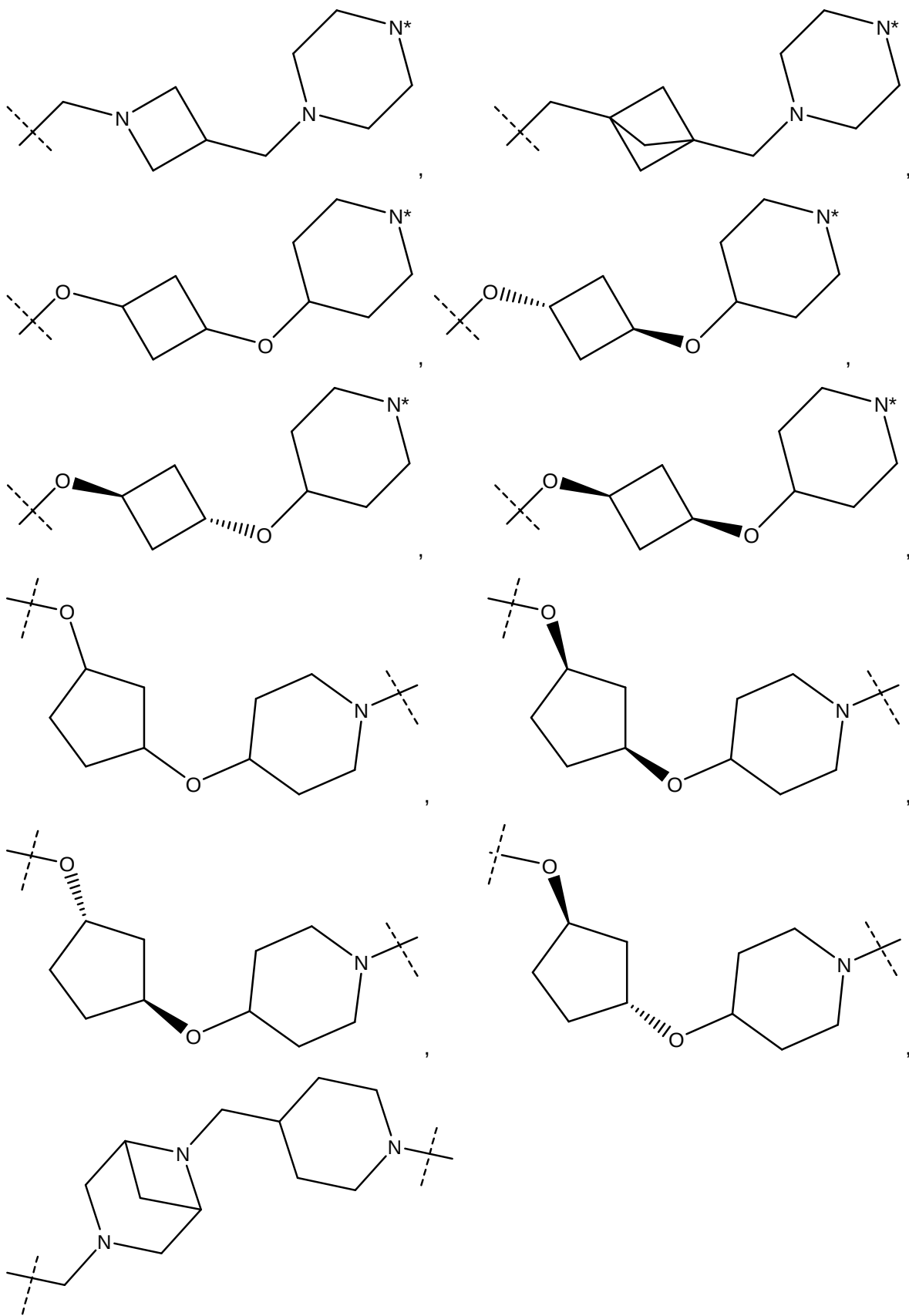


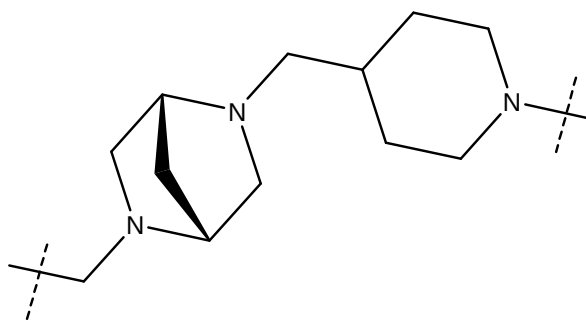
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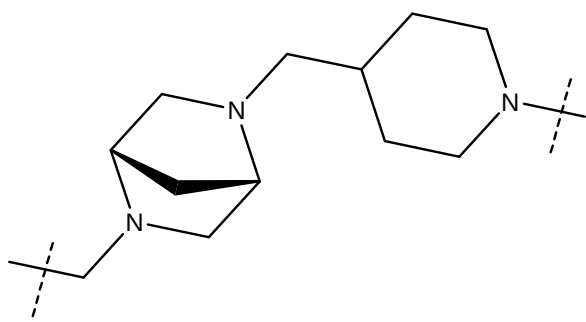
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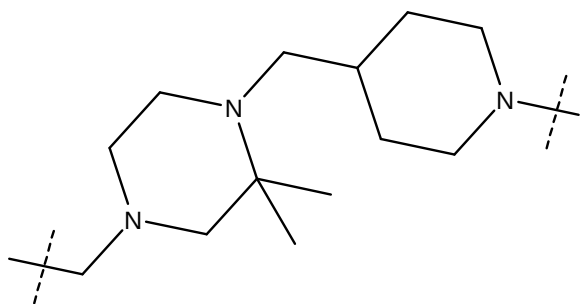




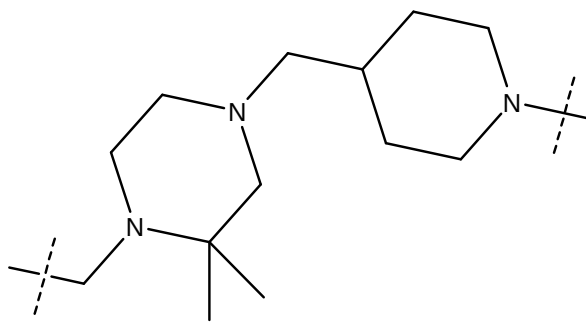
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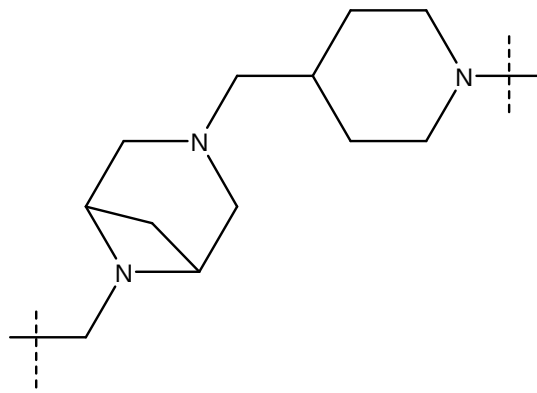
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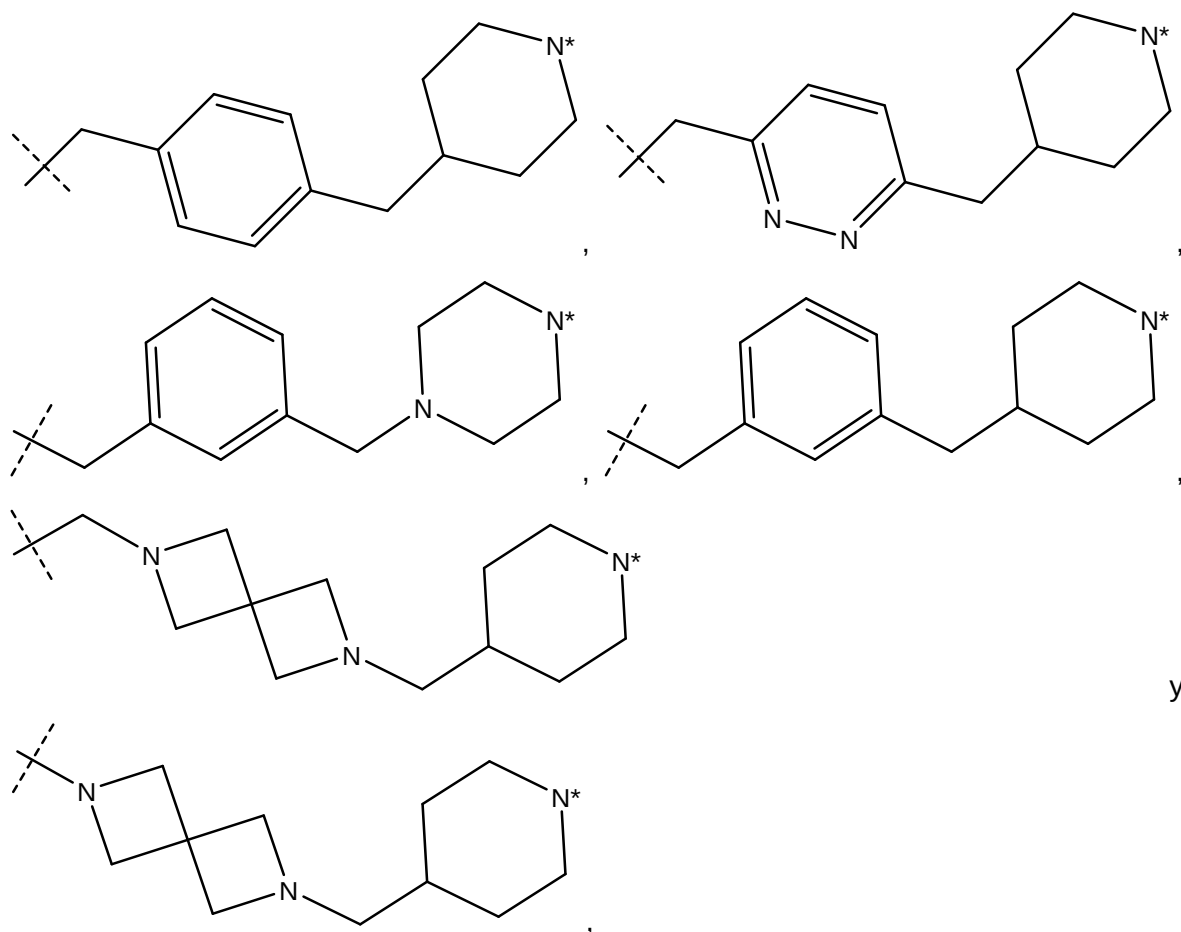
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y

en donde:

N* es un átomo de nitrógeno que está unido covalentemente o compartido con el CLM o el PTM; y

y representaron el punto de unión al CLM o al PTM; o

(d) una combinación de estos.

21. El compuesto de la reivindicación 1, en donde al menos uno de:

la PTM es una PTM que se selecciona de los compuestos 52-288;

la CLM es una CLM que se selecciona de los compuestos 52-288; y

la L es una L que se selecciona de los compuestos 52-288.

22. El compuesto de cualquiera de las reivindicaciones 1-15, en donde uno o más de:

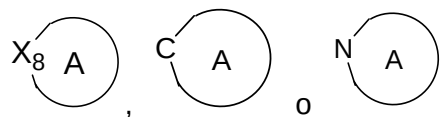
G es H o alquilo C₁₋₆ lineal o ramificado no sustituido o sustituido;

A es H o alquilo C₁₋₆ lineal o ramificado no sustituido o sustituido;

R es un enlace, H, O, -CONR'R'', -C(=O)R', -OR', -NR'R'', alquilo C₁₋₆ lineal o ramificado no sustituido o sustituido, grupo alcoxilo C₁₋₆ opcionalmente sustituido, -Cl, -F, -Br, -CF₃ o -CN,

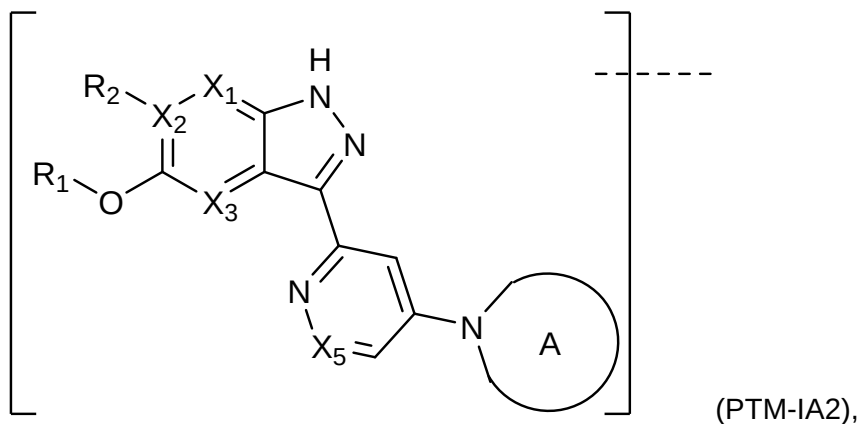
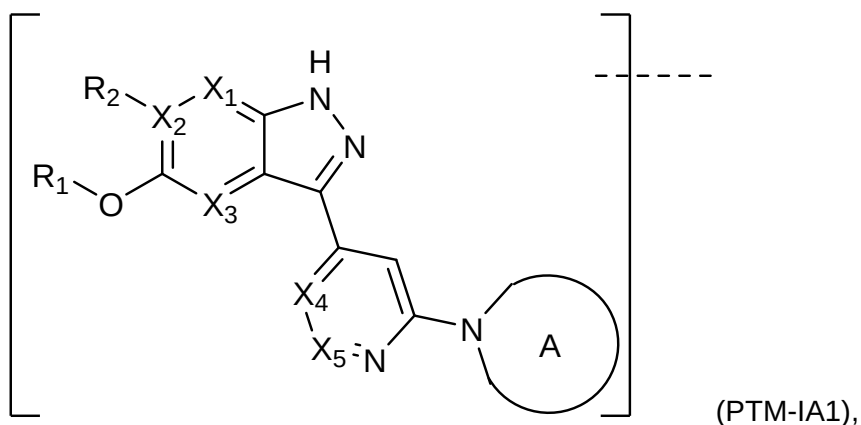
en donde un R está unido covalentemente al L;

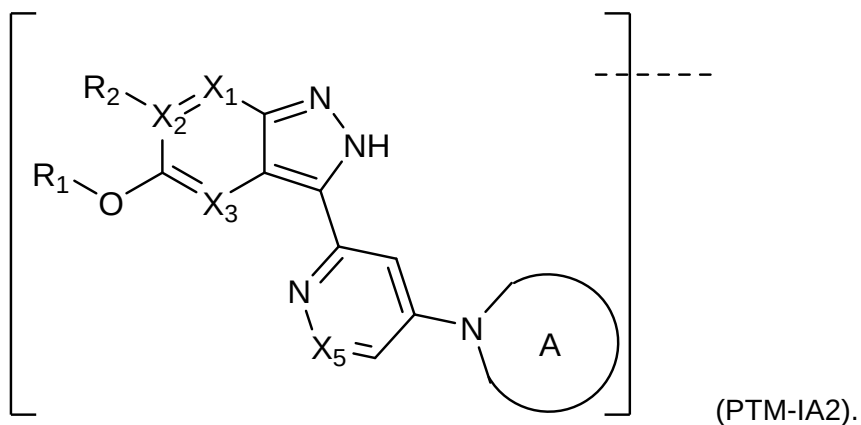
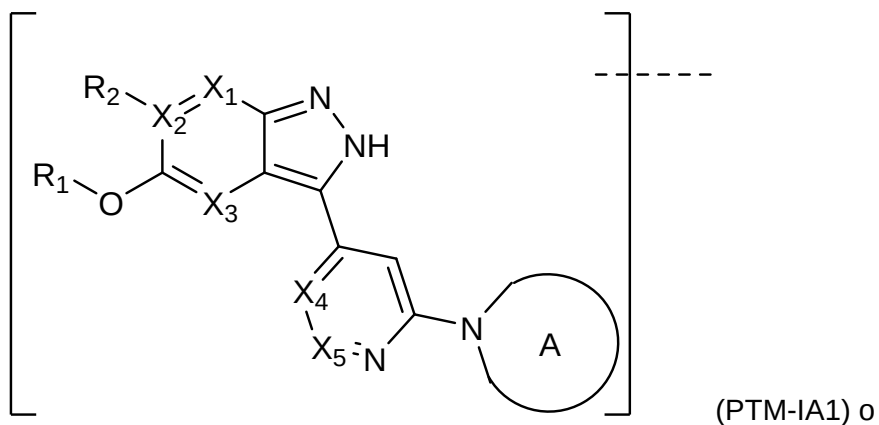
R' y R'' se seleccionan independientemente de un enlace, H y alquilo opcionalmente sustituido con C₁₋₆; y



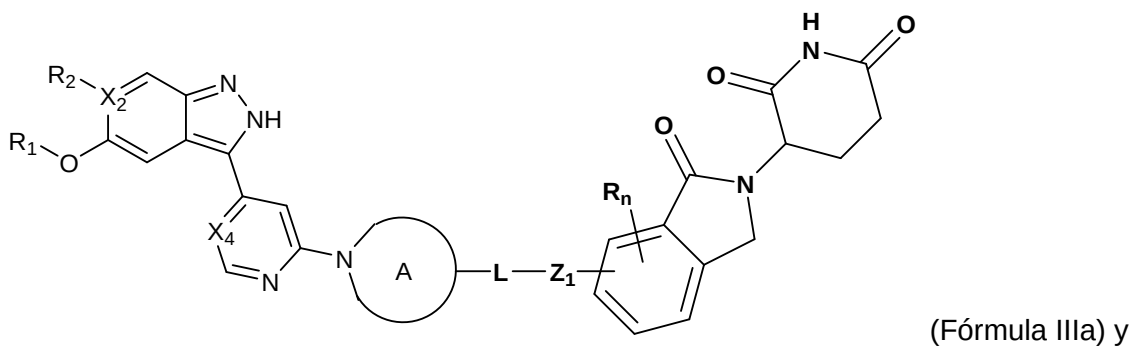
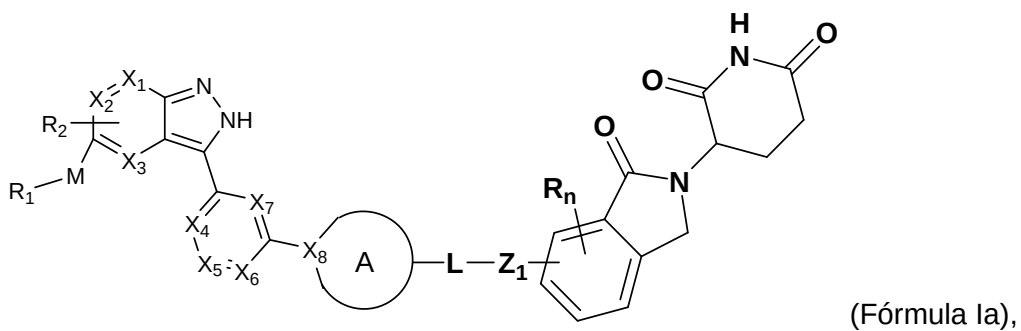
es un cicloalquilo de 3-10 miembros opcionalmente sustituido, heterocicloalquilo de 3-10 miembros opcionalmente sustituido que contiene de 1 a 4 (por ejemplo, 1, 2, 3 o 4) heteroátomos, bicicloalquilo de 3-10 miembros opcionalmente sustituido, biheterocicloalquilo de 3-10 miembros opcionalmente sustituido que contiene de 1 a 4 (por ejemplo, 1, 2, 3 o 4) heteroátomos, espirocicloalquilo de 3-10 miembros opcionalmente sustituido o espiroheterocicloalquilo de 3-10 miembros opcionalmente sustituido que contiene de 1 a 4 (por ejemplo, 1, 2, 3 o 4) heteroátomos, en donde los heteroátomos se seleccionan independientemente de N, O y S.

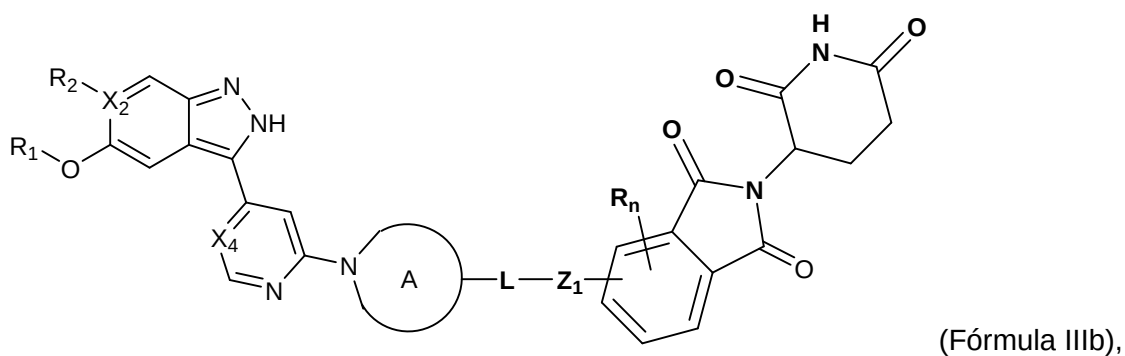
23. El compuesto de cualquiera de las reivindicaciones 1, 4 y 22, en donde el PTM tiene la estructura química:





24. El compuesto de cualquiera de las reivindicaciones 1, 4 y 23, en donde el compuesto tiene la estructura química:





en donde:

X₂ es C, CH o N;

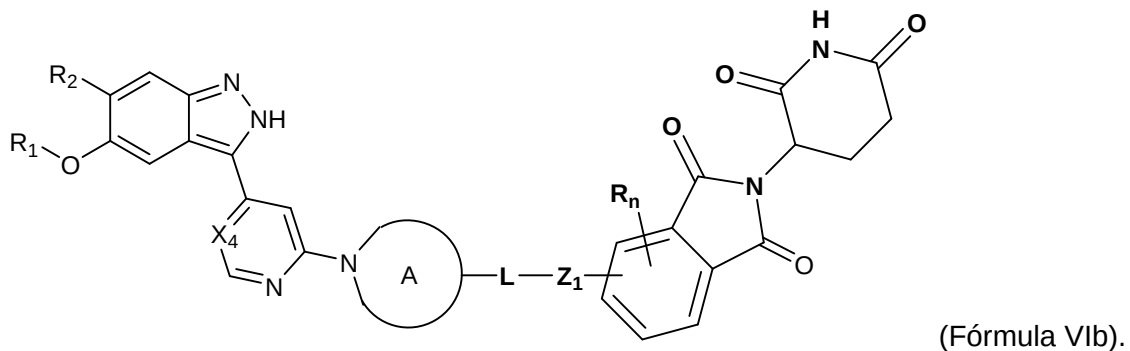
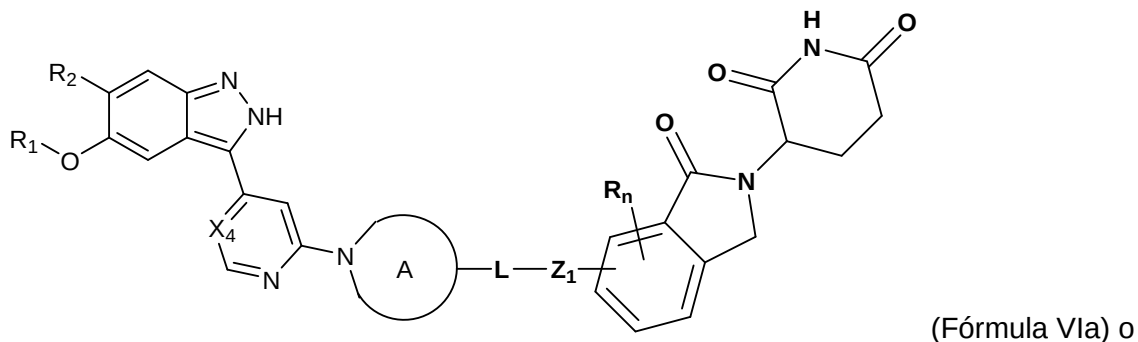
Z₁ es un enlace, un carbono compartido con un grupo cíclico de L o un nitrógeno compartido con un grupo cíclico de L;

n es un número entero de 0 a 3 (por ejemplo, 0, 1, 2 o 3);

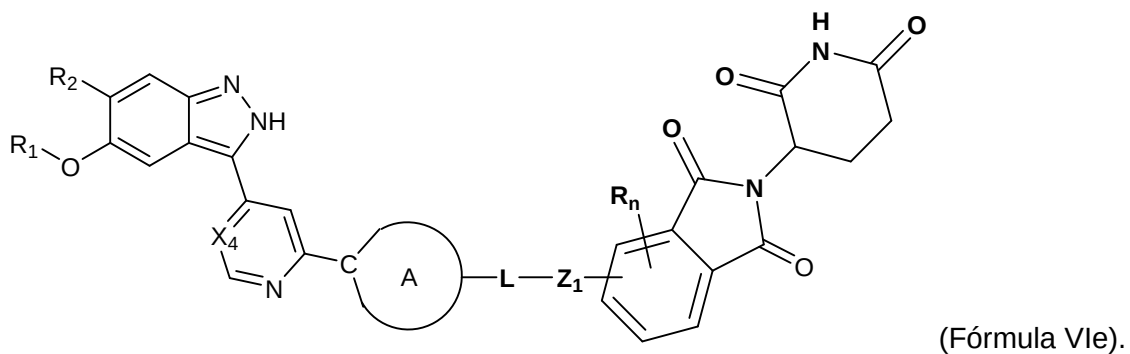
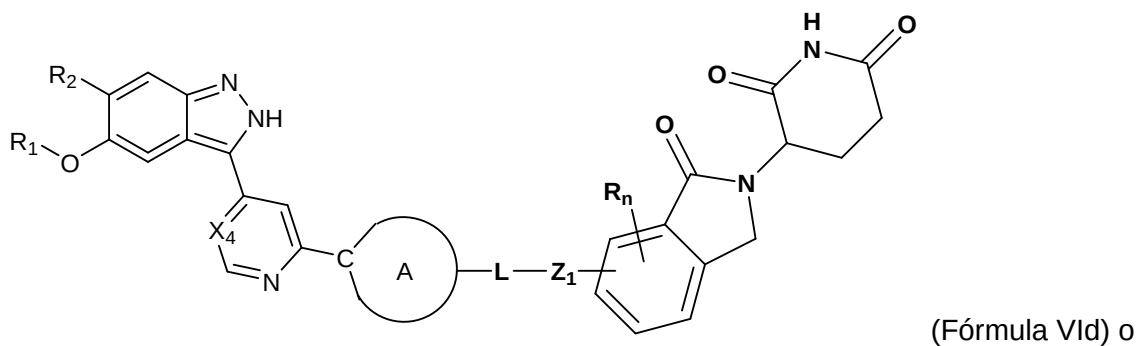
R es un enlace, H, O, OH, N, NH, NH₂, Cl, -F, metilo, metoxi o etoxi; y

R² es H, Cl, F, OH, alquilo C1-C3 o fluoralquilo C1-3.

25. El compuesto de la reivindicación 24, en donde el compuesto está representado por la estructura química:



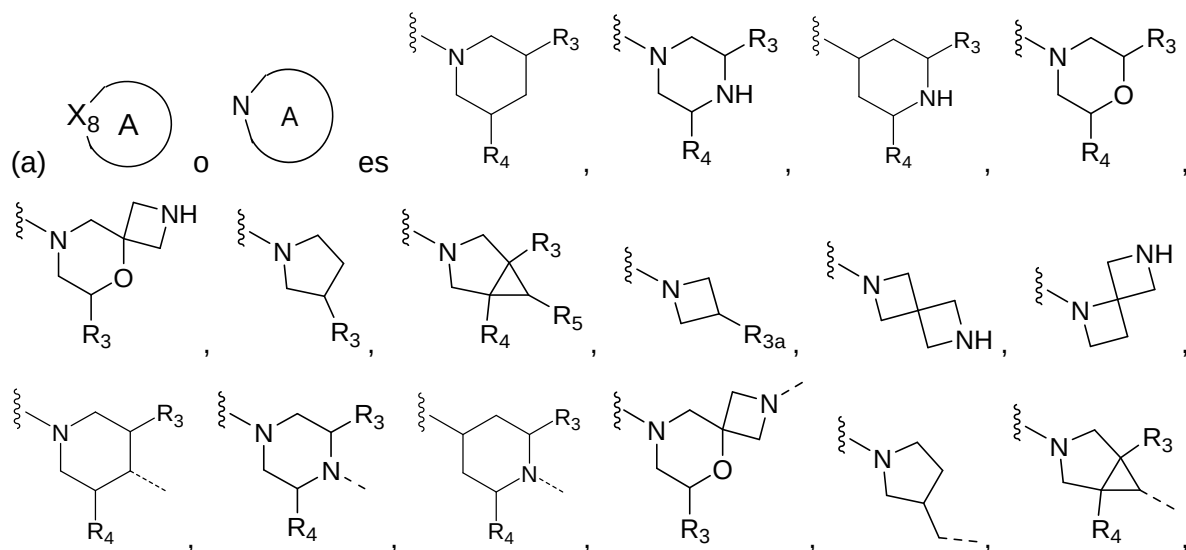
26. El compuesto de la reivindicación 24, en donde el compuesto está representado por la estructura química:

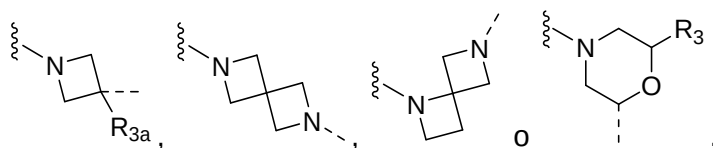


27. El compuesto de cualquiera de las reivindicaciones 23-26, en donde cada R se selecciona de un H, O, OH, NH, NH₂, -Cl, -F, CN, CF₃, alquilo C₁₋₃ lineal o ramificado opcionalmente sustituido, alcoxi C₁₋₃ lineal o ramificado opcionalmente sustituido.

28. El compuesto de cualquiera de las reivindicaciones 23-26, en donde cada R se selecciona de un H, O, OH, NH, NH₂, -Cl, -F, -CN, CF₃, metilo, metoxi y etoxi.

29. El compuesto de cualquiera de las reivindicaciones 23-28, en donde:





en donde:

R₃ es H o metilo;

R_{3a} es H, halógeno o metilo;

R₄ es H o metilo;

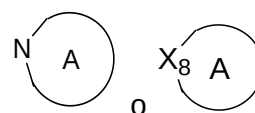
R₅ es H o metilo;

— indica el punto de unión al PTM; y

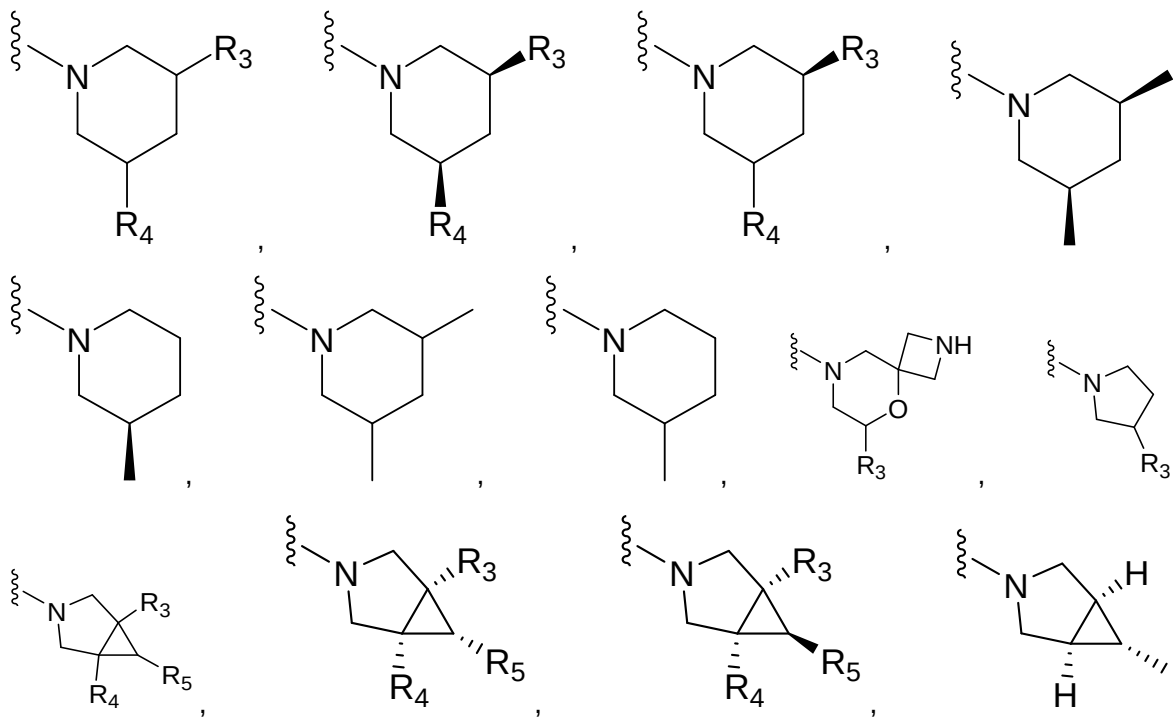
— indica el punto de unión con la L, y donde — no está presente, la está unida a la L a través de un átomo de un N o CH del grupo cíclico, R₃, R₄ o R₅;

(b) R₂ es H o F; o

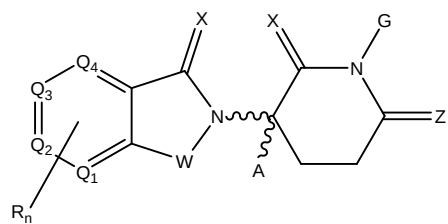
(c) una combinación de estos.



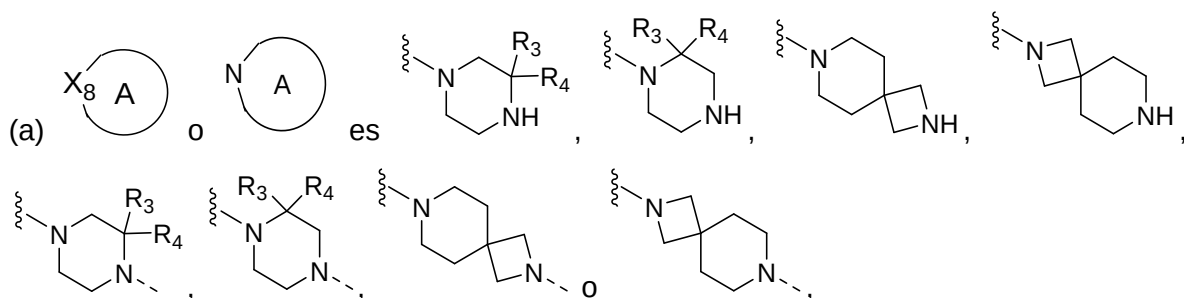
30. El compuesto de cualquiera de las reivindicaciones 23-29, en donde se selecciona del grupo que consiste en:



31. El compuesto de cualquiera de las reivindicaciones 1-15 y 22-30, en donde la CLM tiene una estructura química representada por:



32. El compuesto de cualquiera de las reivindicaciones 1-13 y 22-31, en donde:



en donde:

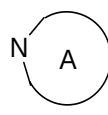
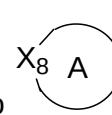
R_3 es H o metilo;

R_{3a} es H, halógeno o metilo;

R_4 es H o metilo;

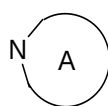
R_5 es H o metilo;

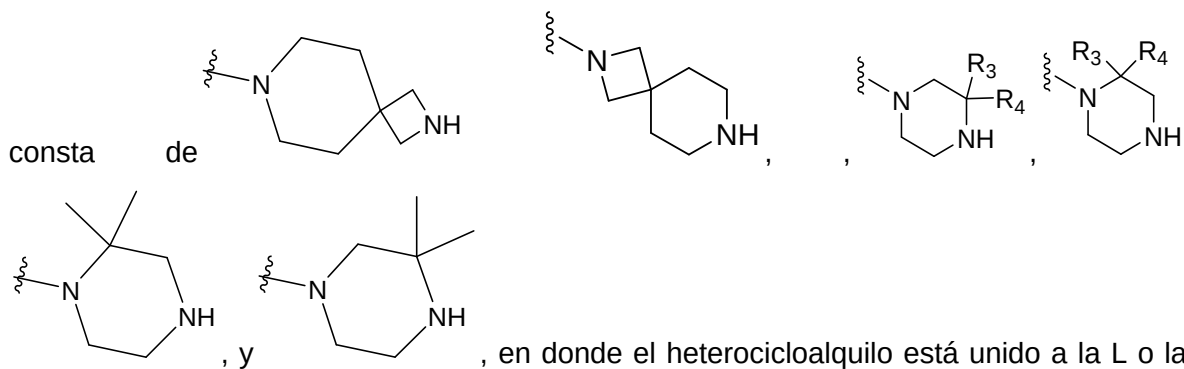
 indica el punto de unión al PTM; y

 indica el punto de unión con la L, y donde  no está presente, la  o  está unida a la L a través de un átomo de un N o CH del grupo cíclico, R_3 o R_4 ;

(b) R_2 es H o F; o

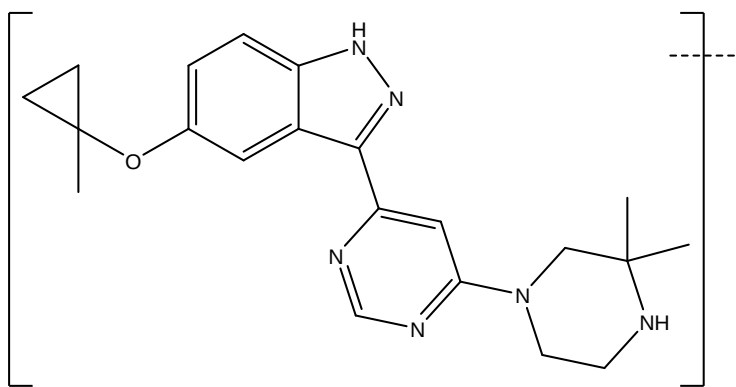
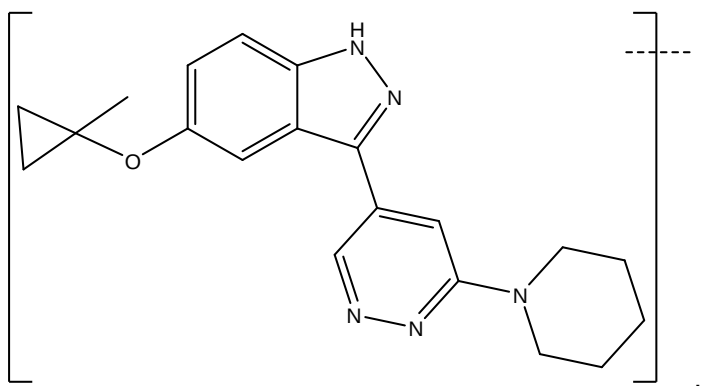
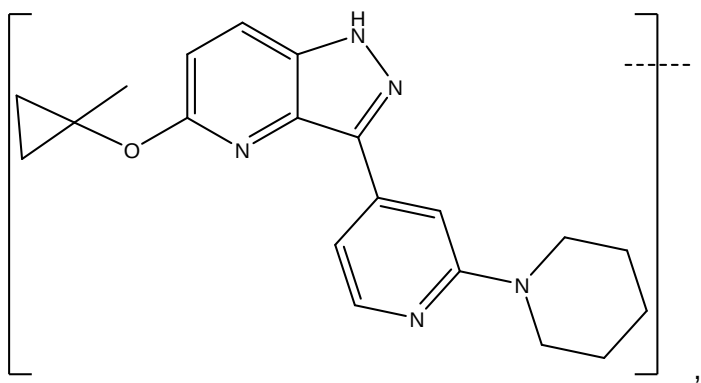
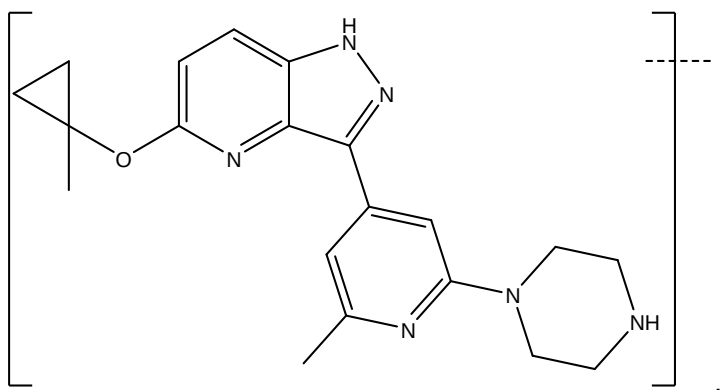
(c) una combinación de estos.

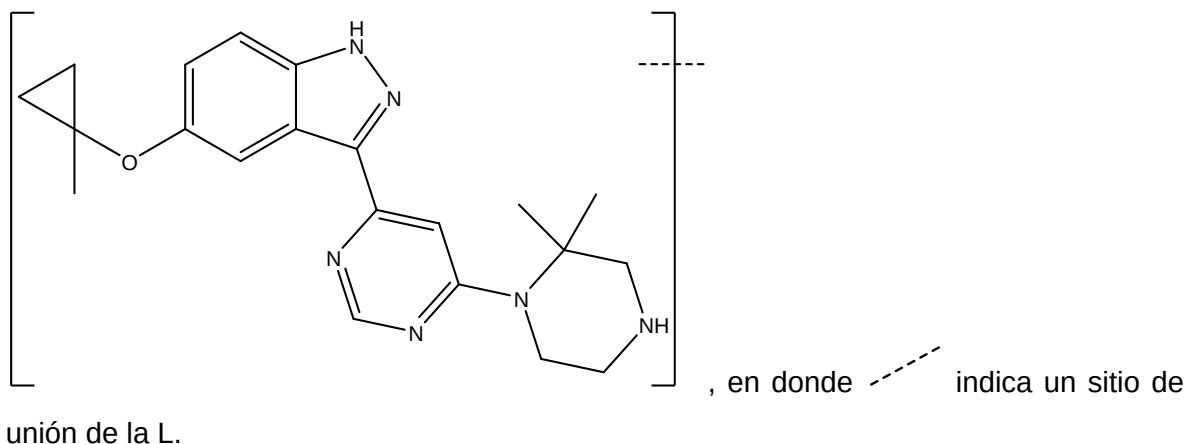
33. El compuesto de la reivindicación 32, en donde  se selecciona del grupo que



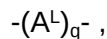
PTM a través de un átomo del grupo cíclico o un sustituyente de este.

34. El compuesto de cualquiera de las reivindicaciones 1-13 y 22, en donde la PTM está representada por una estructura química:





35. El compuesto de cualquiera de las reivindicaciones 23-34, en donde L comprende una unidad estructural química representada por la fórmula:



en donde:

$-(A^L)_q-$ es un grupo que está conectado al CLM y al PTM;

q es un número entero igual o superior a 1;

cada A^L se selecciona independientemente de $CR^{L1}R^{L2}$, O, S, SO, SO_2 , NR^{L3} , SO_2NR^{L3} , $SONR^{L3}$, $CONR^{L3}$, $NR^{L3}CONR^{L4}$, $NR^{L3}SO_2NR^{L4}$, CO, $CR^{L1}=CR^{L2}$, $C\equiv C$, cicloalquilo C_{3-11} opcionalmente sustituido con 1-6 grupos R^{L1} y/o R^{L2} , espirocicloalquilo C_{5-13} opcionalmente sustituido con 1-9 grupos R^{L1} y/o R^{L2} , heteociclilo C_{3-11} opcionalmente sustituido con 1-6 grupos R^{L1} y/o R^{L2} , espiroheterociclilo C_{5-13} opcionalmente sustituido con 1-8 grupos R^{L1} y/o R^{L2} , arilo opcionalmente sustituido con 0-6 grupos R^{L1} y/o R^{L2} , y heteroarilo opcionalmente sustituido con 1-6 grupos R^{L1} y/o R^{L2} ; y

R^{L1} , R^{L2} , R^{L3} , R^{L4} y R^{L5} son, cada uno independientemente, H, halógeno, C_{1-8} alquilo, OC_{1-8} alquilo, SC_{1-8} alquilo, NHC_{1-8} alquilo, $N(C_{1-8}alquilo)_2$, C_{3-11} cicloalquilo, arilo, heteroarilo, C_{3-11} heterociclilo, OC_{3-8} cicloalquilo, SC_{3-8} cicloalquilo, NHC_{3-8} cicloalquilo, $N(C_{3-8}cicloalquilo)_2$, $N(C_{3-8}cicloalquilo)(C_{1-8}alquilo)$, OH, NH_2 , SH, $SO_2C_{1-8}alquilo$, $P(O)(OC_{1-8}alquilo)(C_{1-8}alquilo)$, $P(O)(OC_{1-8}alquilo)_2$, $CC-C_{1-8}alquilo$, CCH, $CH=CH(C_{1-8}alquilo)$, $C(C_{1-8}alquilo)=CH(C_{1-8}alquilo)$, $C(C_{1-8}alquilo)=C(C_{1-8}alquilo)_2$, $Si(OH)_3$, $Si(C_{1-8}alquilo)_3$, $Si(OH)(C_{1-8}alquilo)_2$, $COC_{1-8}alquilo$, CO_2H , CN, CF_3 , CHF_2 , CH_2F , NO_2 , SF_5 , $SO_2NHC_{1-8}alquilo$, $SO_2N(C_{1-8}alquilo)_2$, $SONHC_{1-8}alquilo$, $SON(C_{1-8}alquilo)_2$, $CONHC_{1-8}alquilo$, $CON(C_{1-8}alquilo)_2$, $N(C_{1-8}alquilo)CONH(C_{1-8}alquilo)$, $N(C_{1-8}alquilo)CON(C_{1-8}alquilo)_2$, $NHCONH(C_{1-8}alquilo)$, $NHCON(C_{1-8}alquilo)_2$, $NHCONH_2$, $N(C_{1-8}alquilo)SO_2NH(C_{1-8}alquilo)$, $N(C_{1-8}alquilo)SO_2N(C_{1-8}alquilo)_2$, $NH SO_2NH(C_{1-8}alquilo)$, $NH SO_2N(C_{1-8}alquilo)_2$ o $NH SO_2NH_2$.

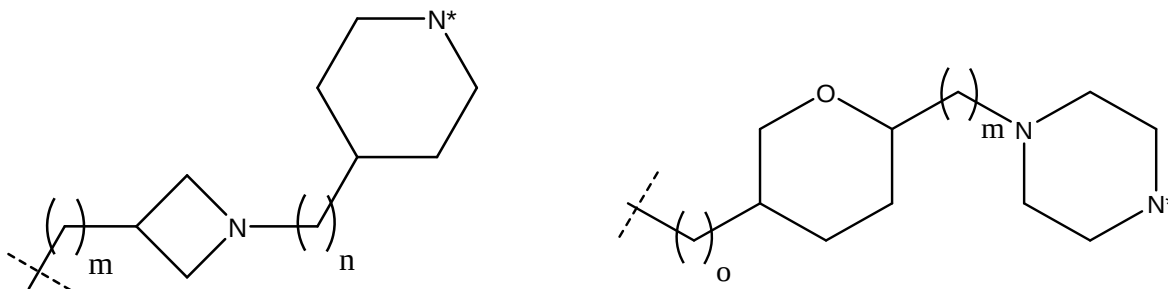
36. El compuesto de cualquiera de las reivindicaciones 23-34, en donde L incluye un alquilo

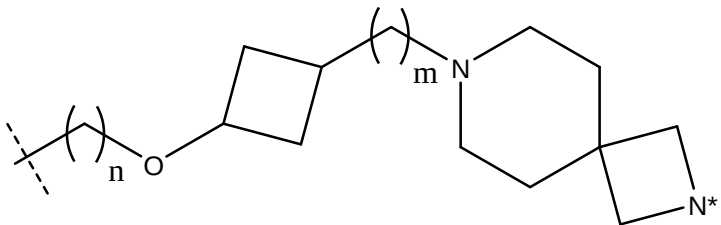
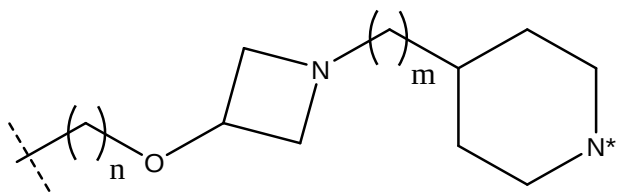
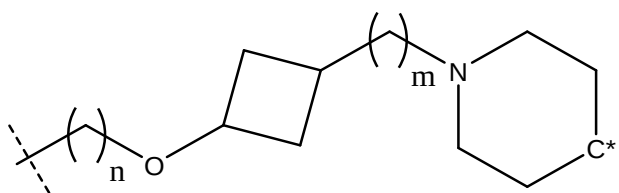
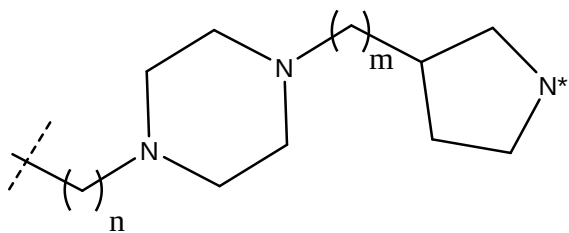
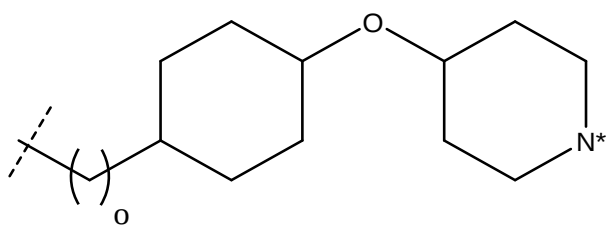
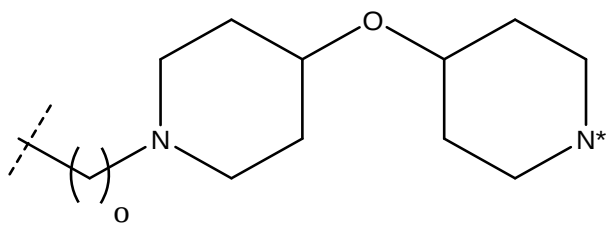
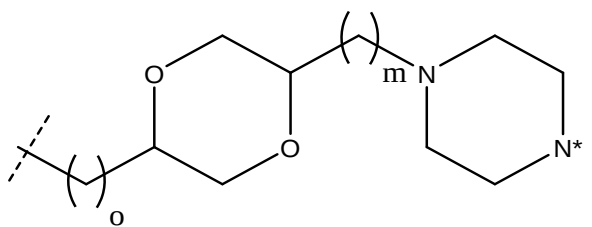
C₁-C₅₀ opcionalmente sustituido (por ejemplo, alquilo C₁, C₂, C₃, C₄, C₅, C₆, C₇, C₈, C₉, C₁₀, C₁₁, C₁₂, C₁₃, C₁₄, C₁₅, C₁₆, C₁₇, C₁₈, C₁₉, C₂₀, C₂₁, C₂₂, C₂₃, C₂₄, C₂₅, C₂₆, C₂₇, C₂₈, C₂₉, C₃₀, C₃₁, C₃₂, C₃₃, C₃₄, C₃₅, C₃₆, C₃₇, C₃₈, C₃₉, C₄₀, C₄₁, C₄₂, C₄₃, C₄₄, C₄₅, C₄₆, C₄₇, C₄₈, C₄₉ o C₅₀), en donde:

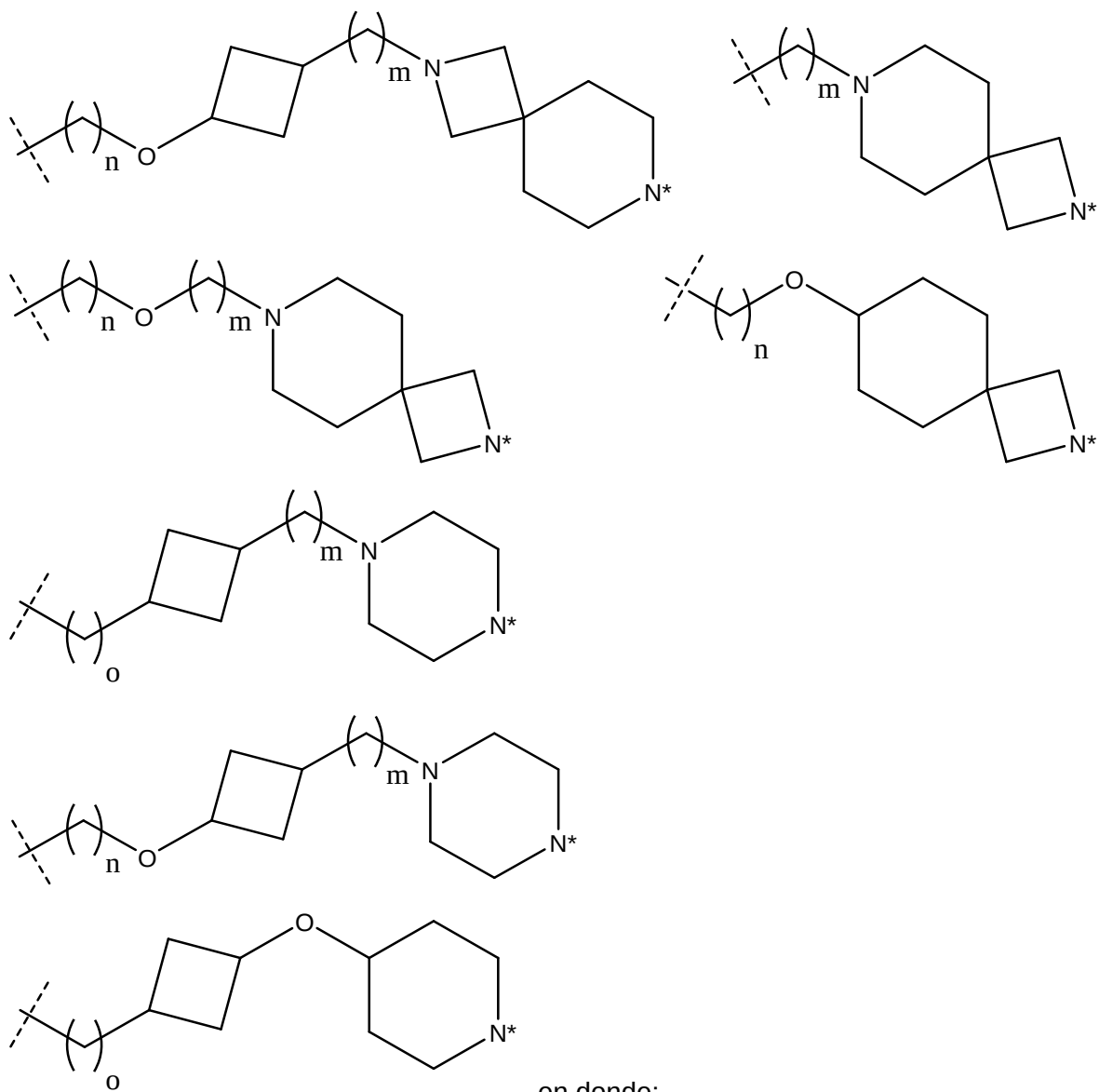
cada carbono se reemplaza opcionalmente con CR^{L1}R^{L2}, O, S, SO, SO₂, NR^{L3}, SO₂NR^{L3}, SONR^{L3}, CONR^{L3}, NR^{L3}CONR^{L4}, NR^{L3}SO₂NR^{L4}, CO, CR^{L1}=CR^{L2}, C≡C, cicloalquilo C₃₋₁₁ opcionalmente sustituido con 1-6 grupos R^{L1} y/o R^{L2}, espirocicloalquilo C₅₋₁₃ opcionalmente sustituido con 1-9 grupos R^{L1} y/o R^{L2}, heteociclilo C₃₋₁₁ opcionalmente sustituido con 1-6 grupos R^{L1} y/o R^{L2}, espiroheterociclilo C₅₋₁₃ opcionalmente sustituido con 1-8 grupos R^{L1} y/o R^{L2}, arilo opcionalmente sustituido con 1-6 grupos R^{L1} y/o R^{L2}, o heteroarilo opcionalmente sustituido con 1-6 grupos R^{L1} y/o R^{L2}; y

R^{L1}, R^{L2}, R^{L3}, R^{L4} y R^{L5} son, cada uno independientemente, H, halógeno, C₁₋₈alquilo, OC₁₋₈alquilo, SC₁₋₈alquilo, NHC₁₋₈alquilo, N(C₁₋₈alquilo)₂, C₃₋₁₁cicloalquilo, arilo, heteroarilo, C₃₋₁₁heterociclilo, OC₃₋₈cicloalquilo, SC₃₋₈cicloalquilo, NHC₃₋₈cicloalquilo, N(C₃₋₈cicloalquilo)₂, N(C₃₋₈cicloalquilo)(C₁₋₈alquilo), OH, NH₂, SH, SO₂C₁₋₈alquilo, P(O)(OC₁₋₈alquilo)(C₁₋₈alquilo), P(O)(OC₁₋₈alquilo)₂, CC-C₁₋₈alquilo, CCH, CH=CH(C₁₋₈alquilo), C(C₁₋₈alquilo)=CH(C₁₋₈alquilo), C(C₁₋₈alquilo)=C(C₁₋₈alquilo)₂, Si(OH)₃, Si(C₁₋₈alquilo)₃, Si(OH)(C₁₋₈alquilo)₂, COC₁₋₈alquilo, CO₂H, CN, CF₃, CHF₂, CH₂F, NO₂, SF₅, SO₂NHC₁₋₈alquilo, SO₂N(C₁₋₈alquilo)₂, SONHC₁₋₈alquilo, SON(C₁₋₈alquilo)₂, CONHC₁₋₈alquilo, CON(C₁₋₈alquilo)₂, N(C₁₋₈alquilo)CONH(C₁₋₈alquilo), N(C₁₋₈alquilo)CON(C₁₋₈alquilo)₂, NHCONH(C₁₋₈alquilo), NHCON(C₁₋₈alquilo)₂, NHCONH₂, N(C₁₋₈alquilo)SO₂NH(C₁₋₈alquilo), N(C₁₋₈alquilo)SO₂N(C₁₋₈alquilo)₂, NH SO₂NH(C₁₋₈alquilo), NH SO₂N(C₁₋₈alquilo)₂ o NH SO₂NH₂.

37. El compuesto de cualquiera de las reivindicaciones 1-13 y 23-36, en donde L se selecciona del grupo que consiste en:







, en donde:

el grupo enlazador químico está opcionalmente sustituido con 0, 1, 2 o 3 sustituyentes que se seleccionan independientemente de halógeno y metilo (preferentemente halógenos que se seleccionan independientemente);

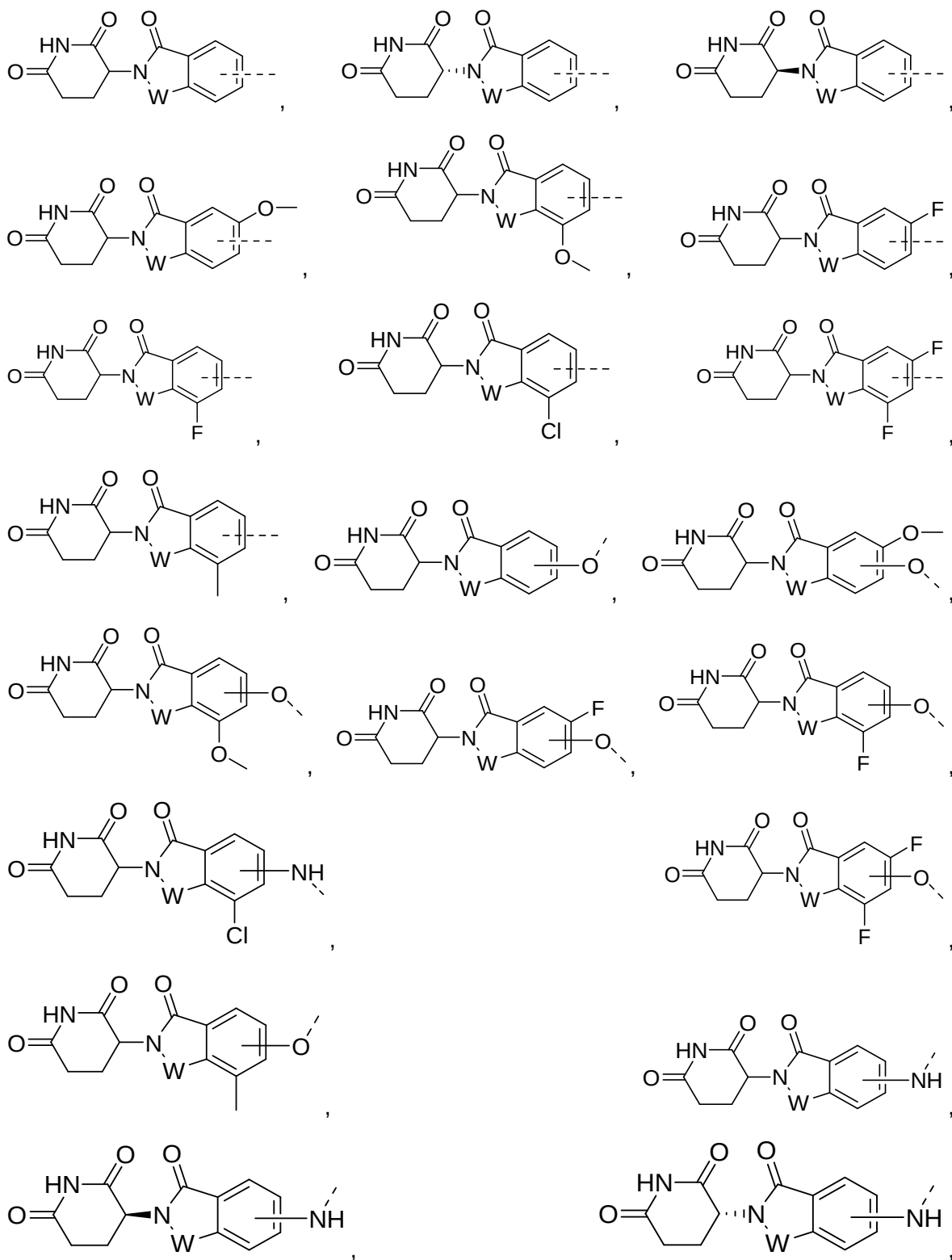
C^* es un átomo de carbono que está unido covalentemente o compartido con el CLM o el PTM;

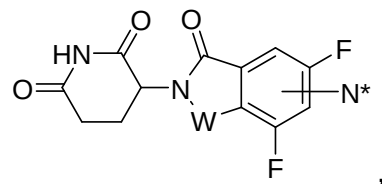
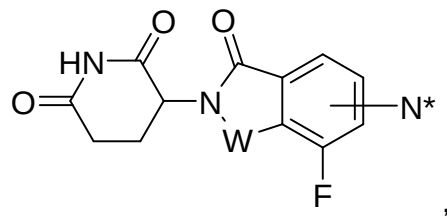
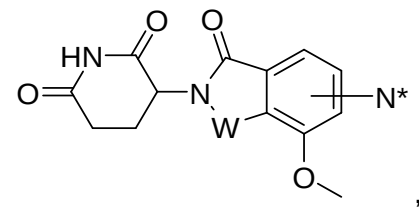
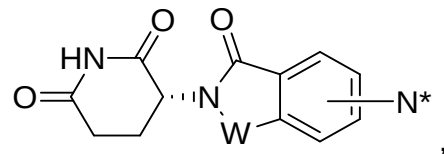
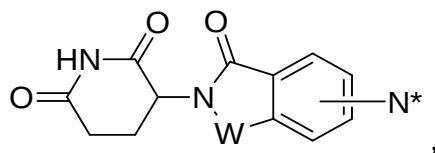
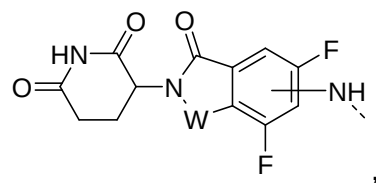
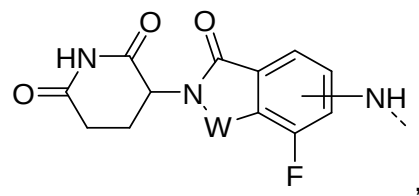
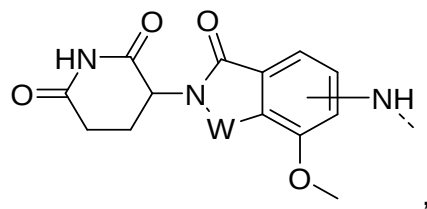
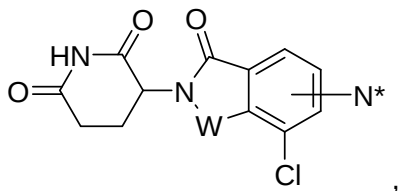
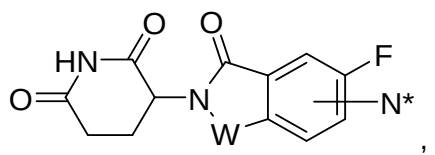
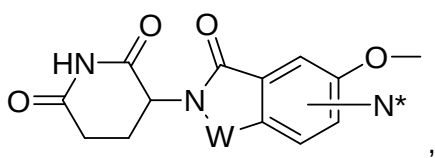
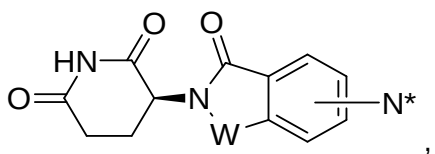
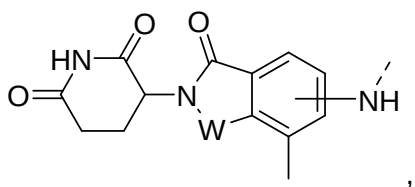
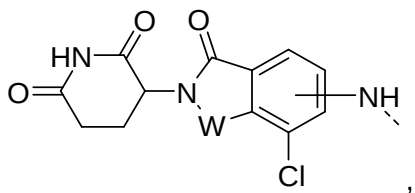
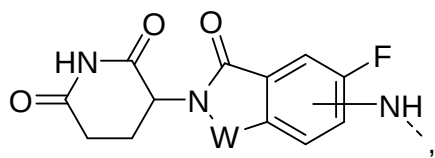
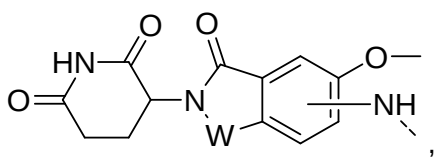
N^* es un átomo de nitrógeno que está unido covalentemente o compartido con el CLM o el PTM; y

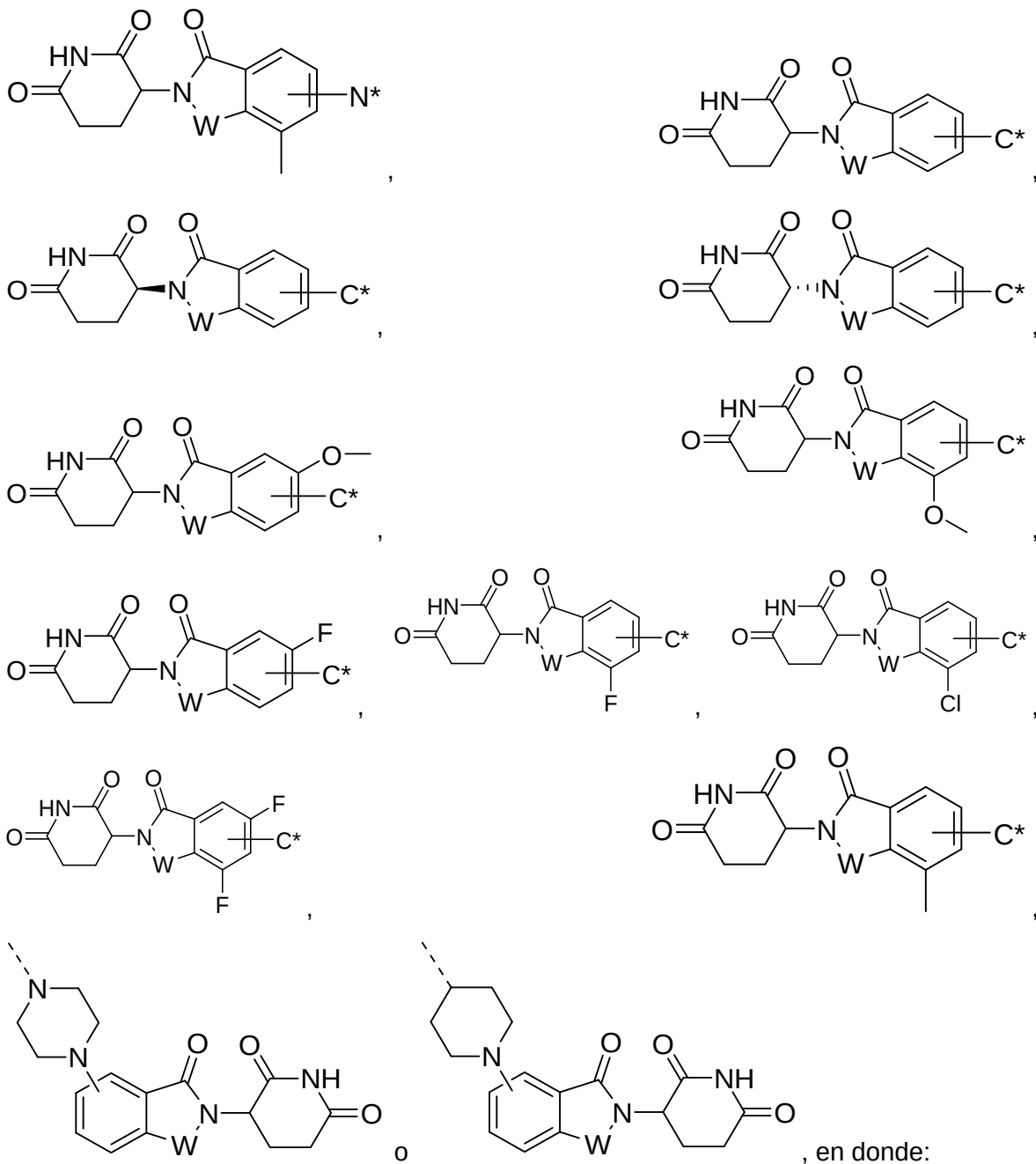
cada m , n y o de L es independientemente 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 o 20.

38. El compuesto de cualquiera de las reivindicaciones 1-37, en donde al menos uno de:

(a) el CLM está representado por:





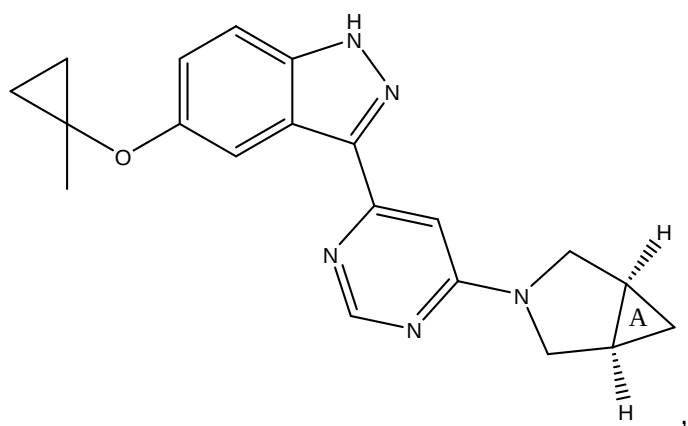
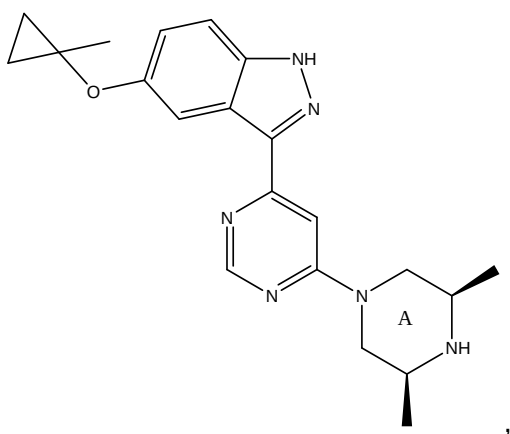
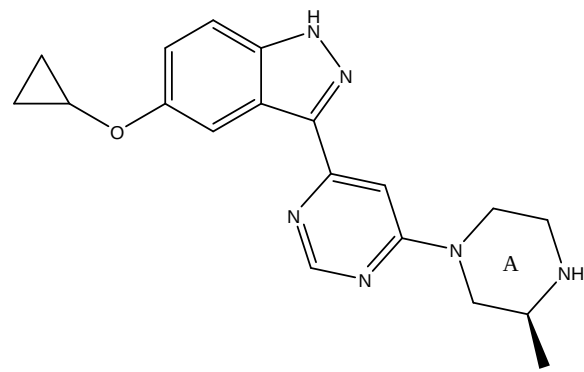
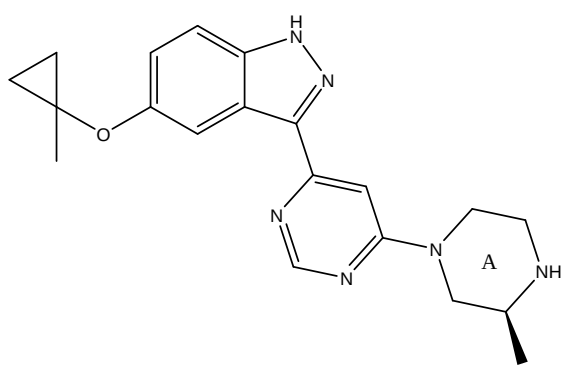
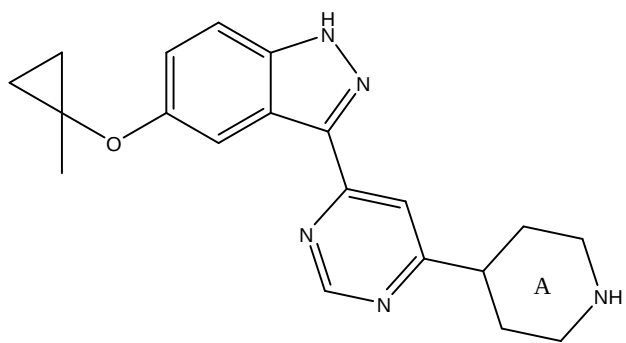


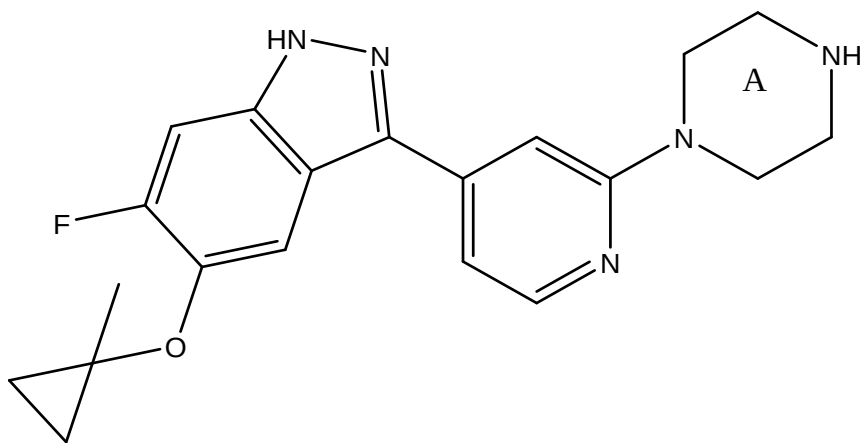
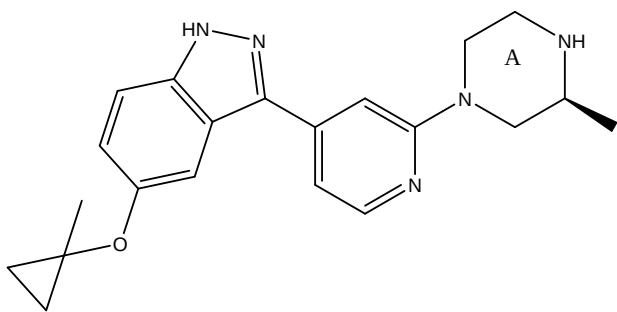
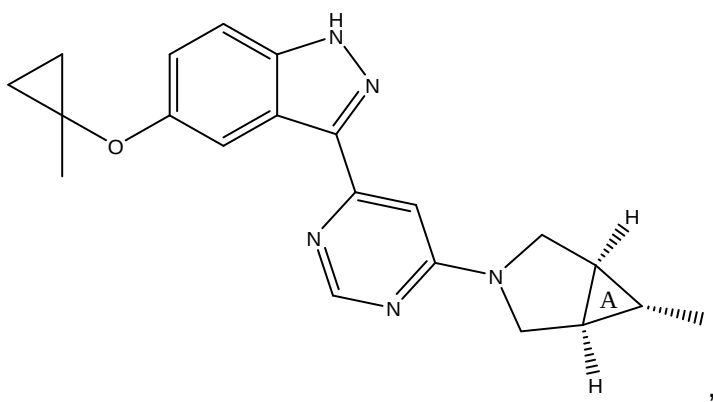
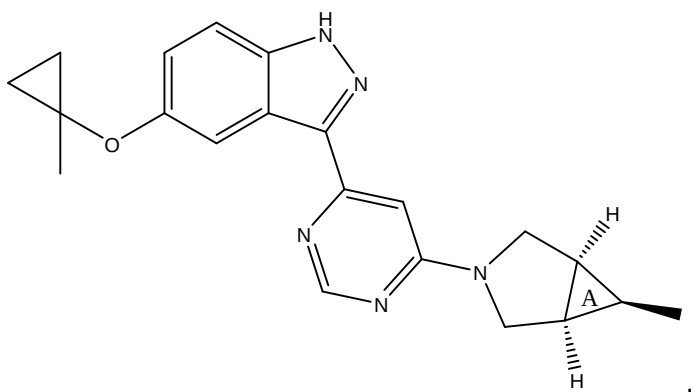
--- de la ULM indica el punto de unión con la L;

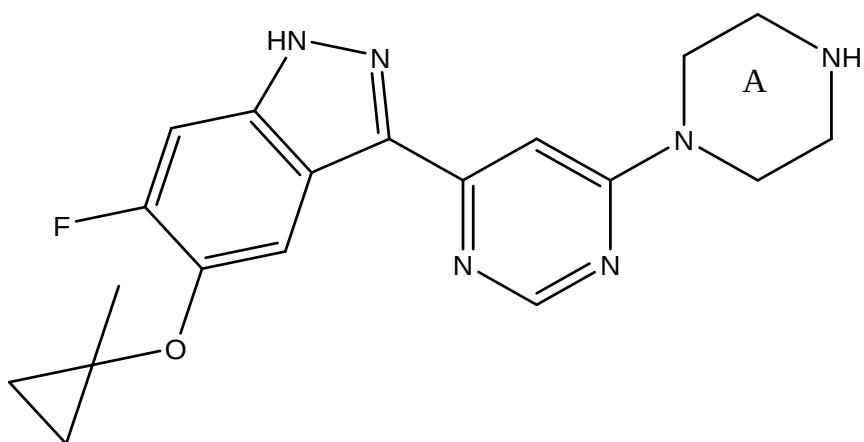
C* es un átomo de carbono que se comparte con el L; y

N* es un átomo de nitrógeno que se comparte con L;

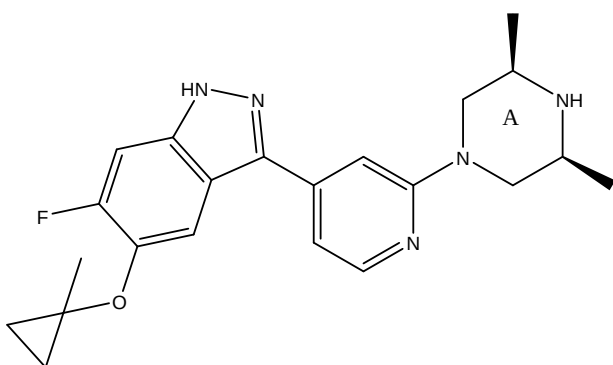
(b) el PTM está representado por:



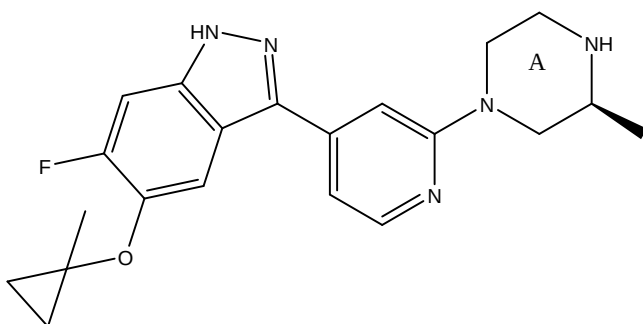




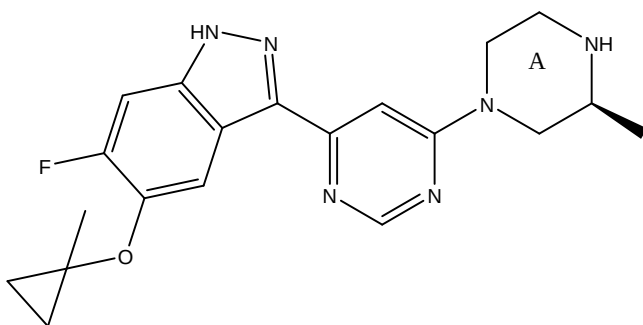
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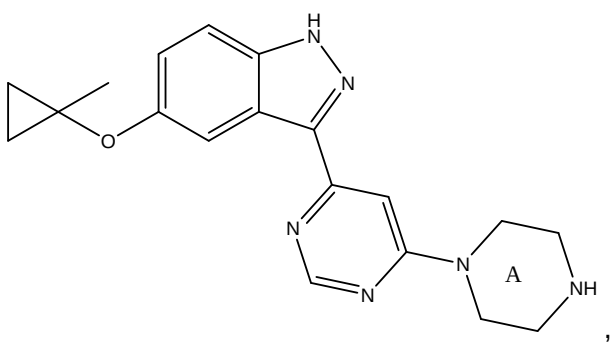
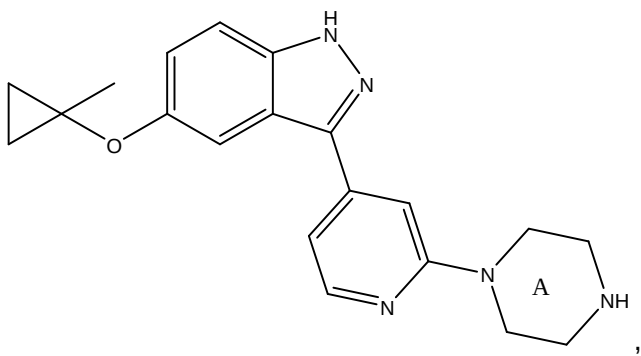
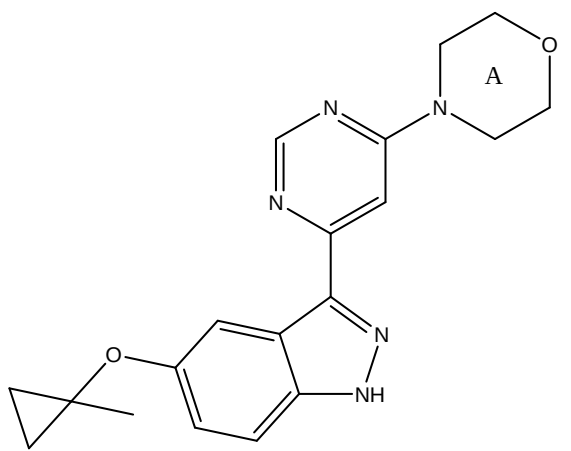
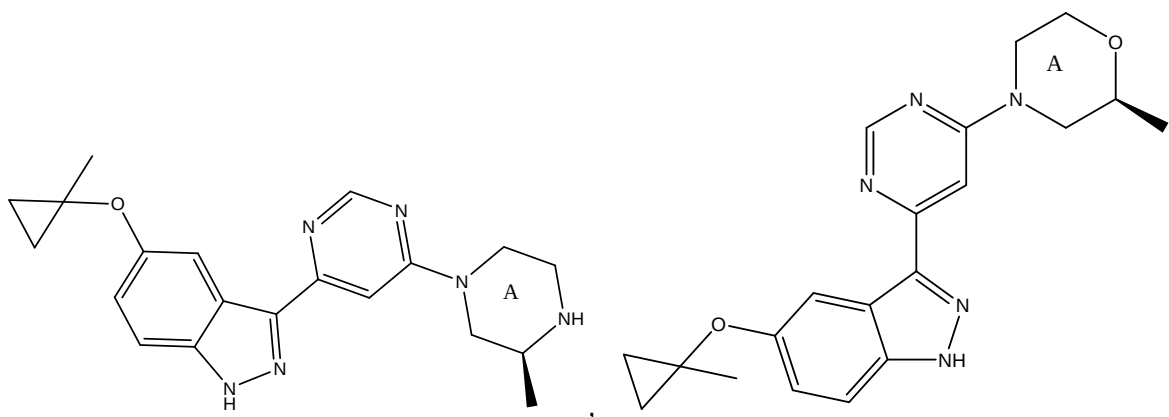
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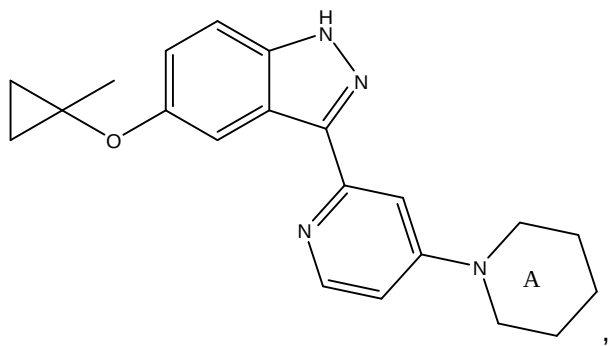
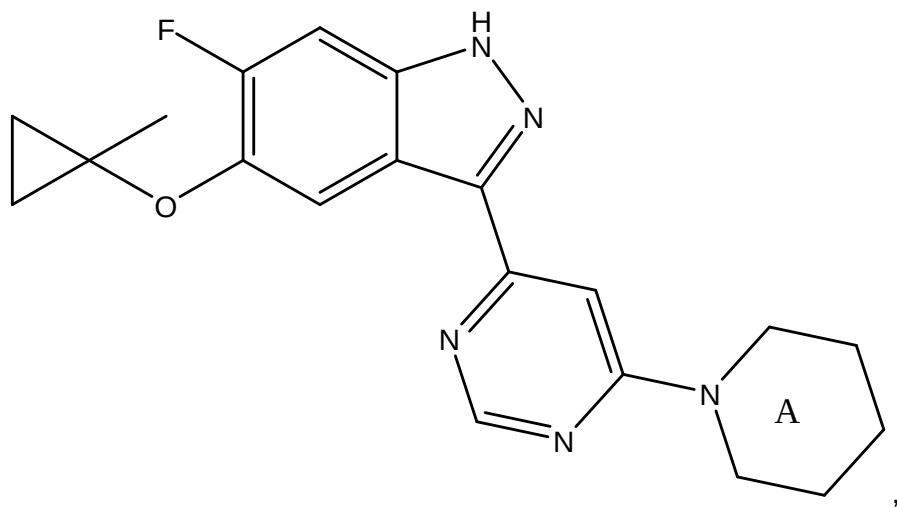
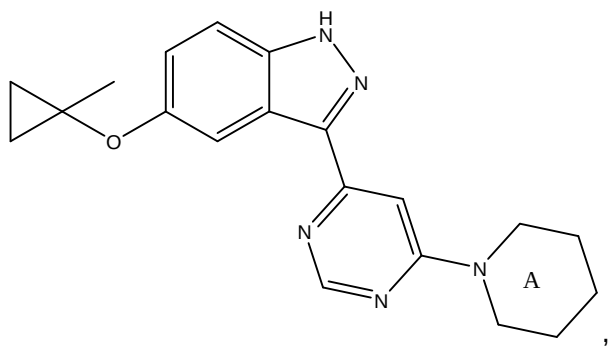
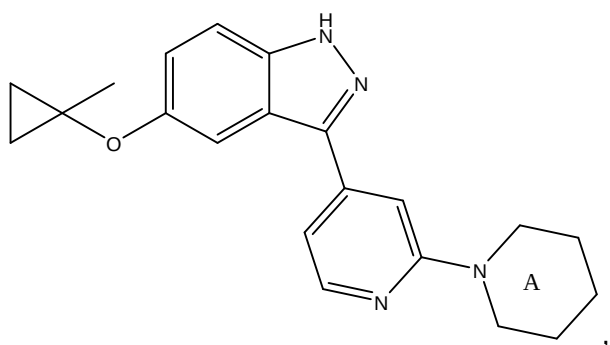


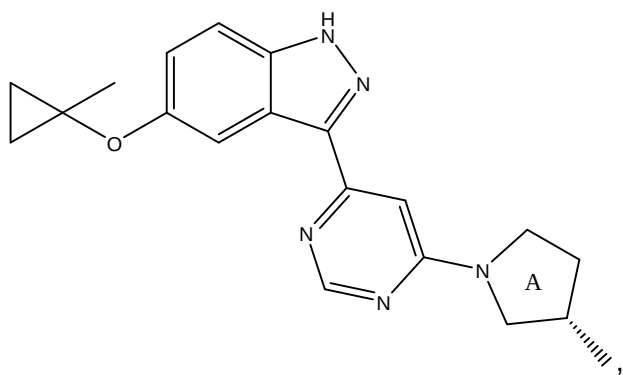
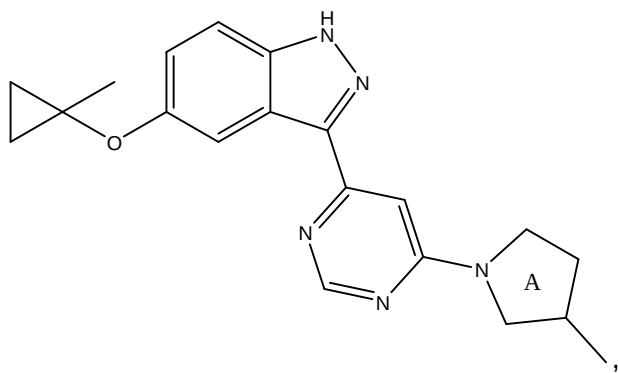
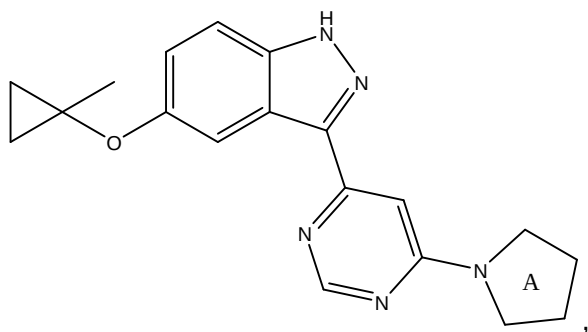
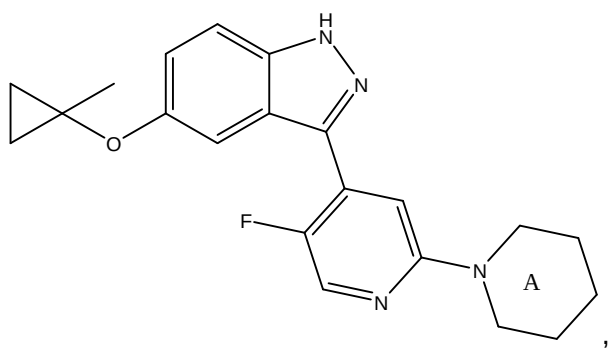
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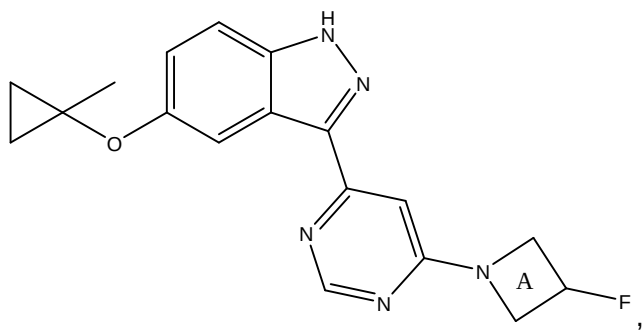
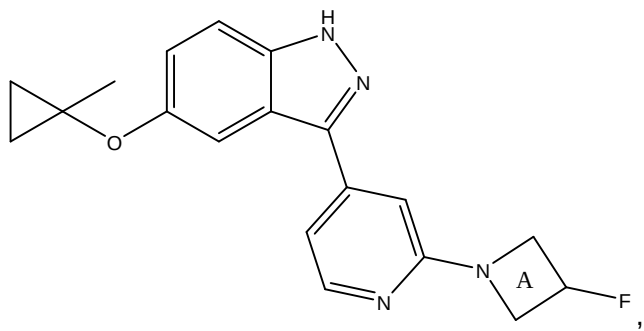
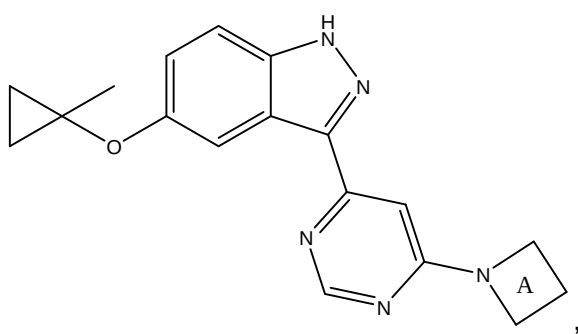
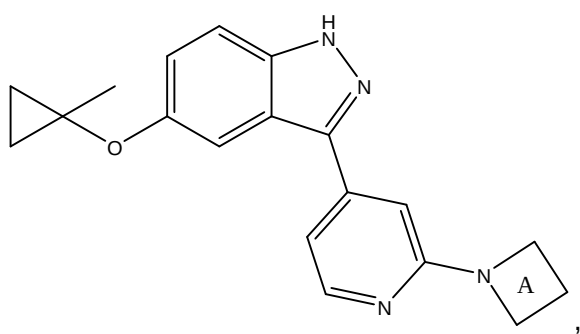
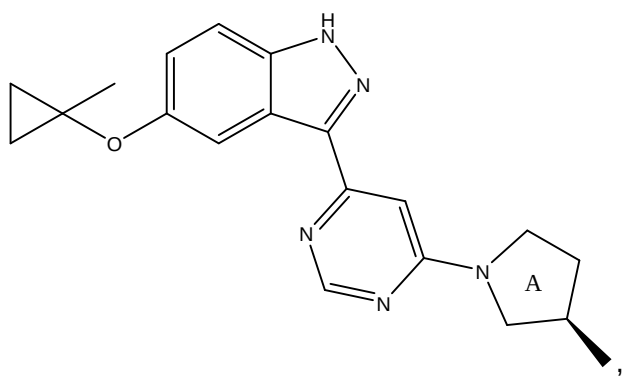


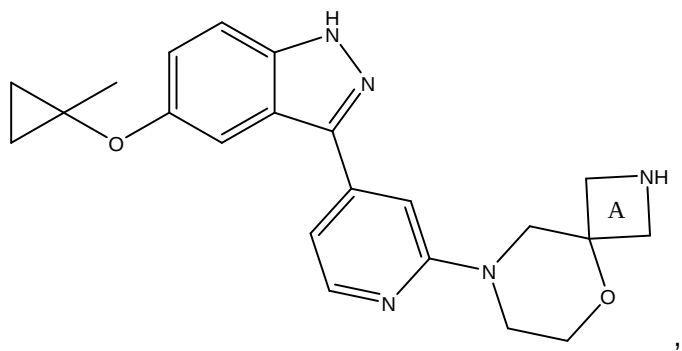
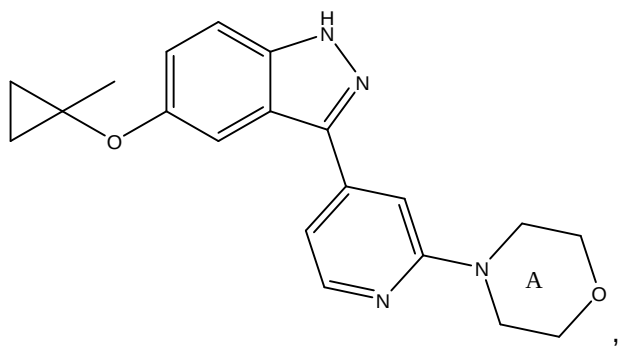
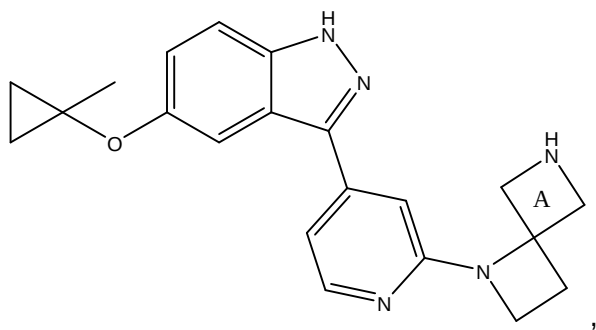
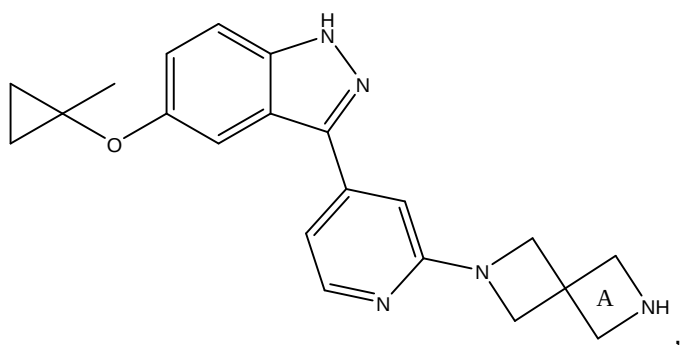
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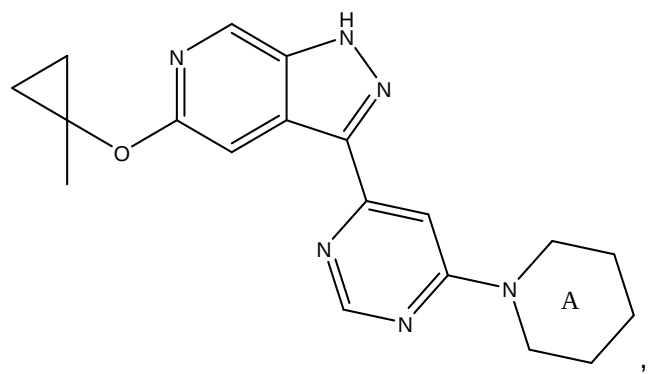
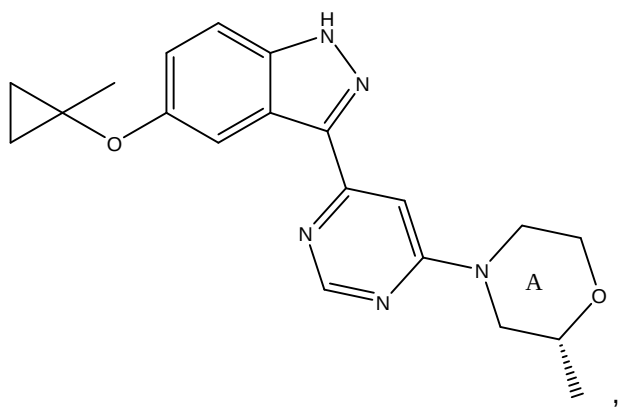
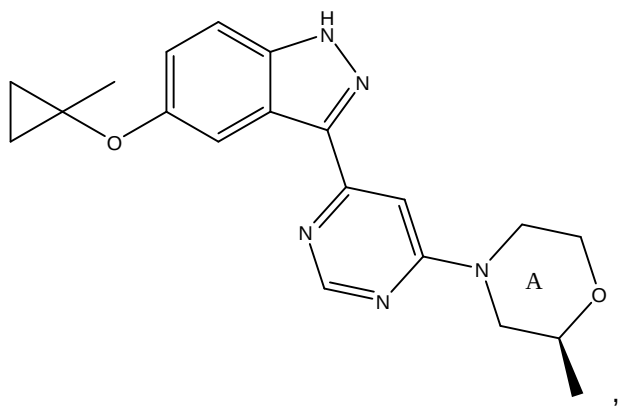
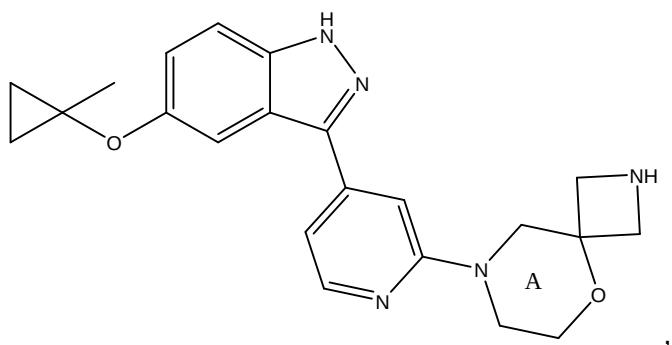


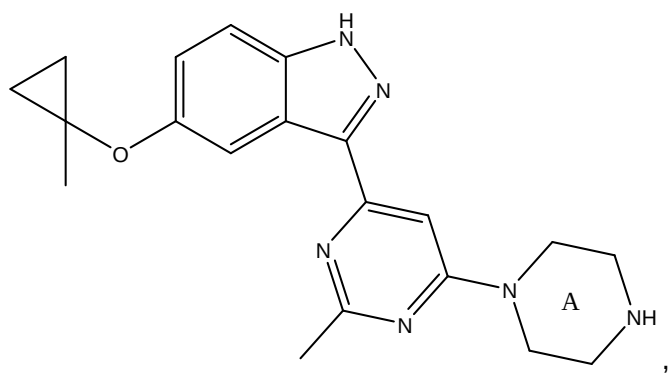
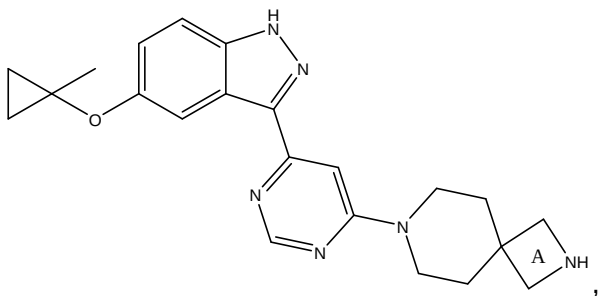
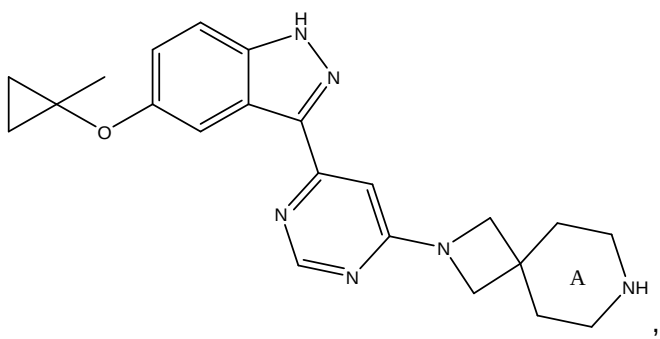
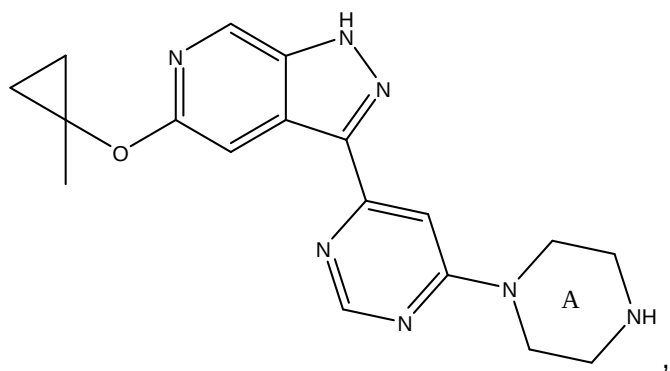


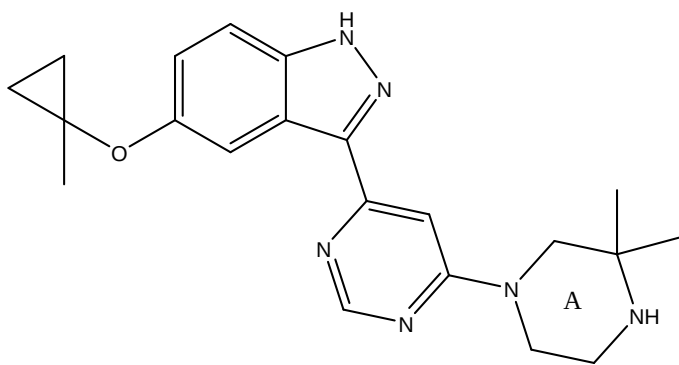
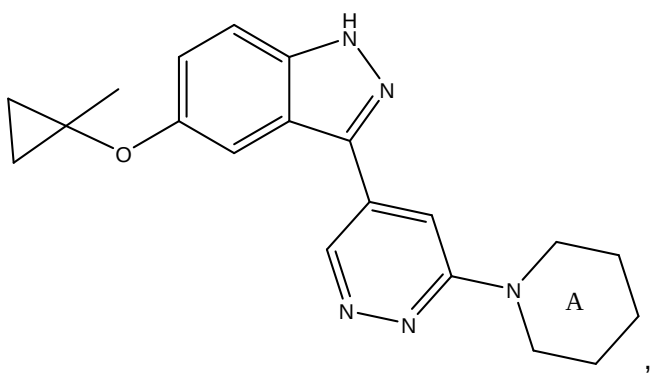
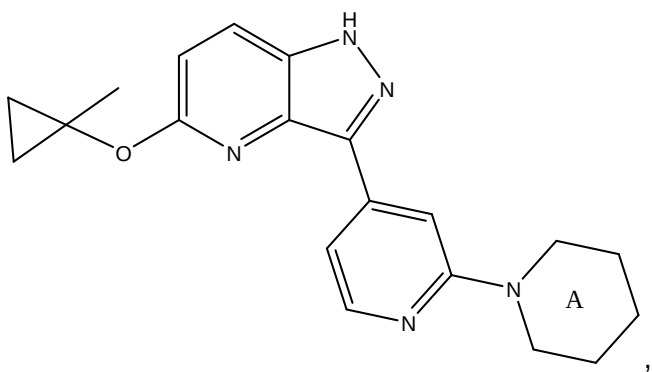
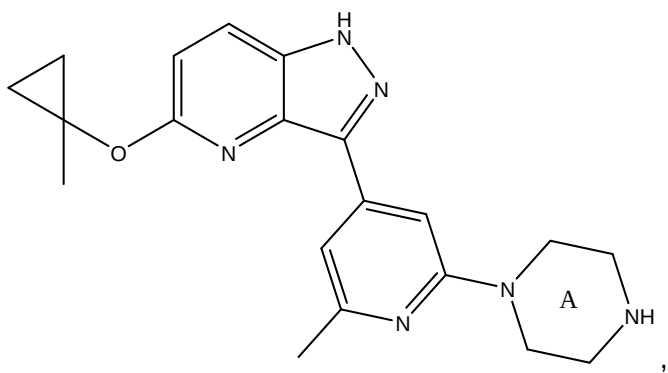


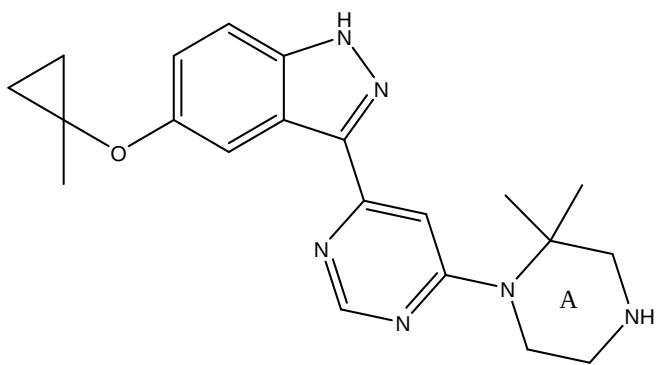






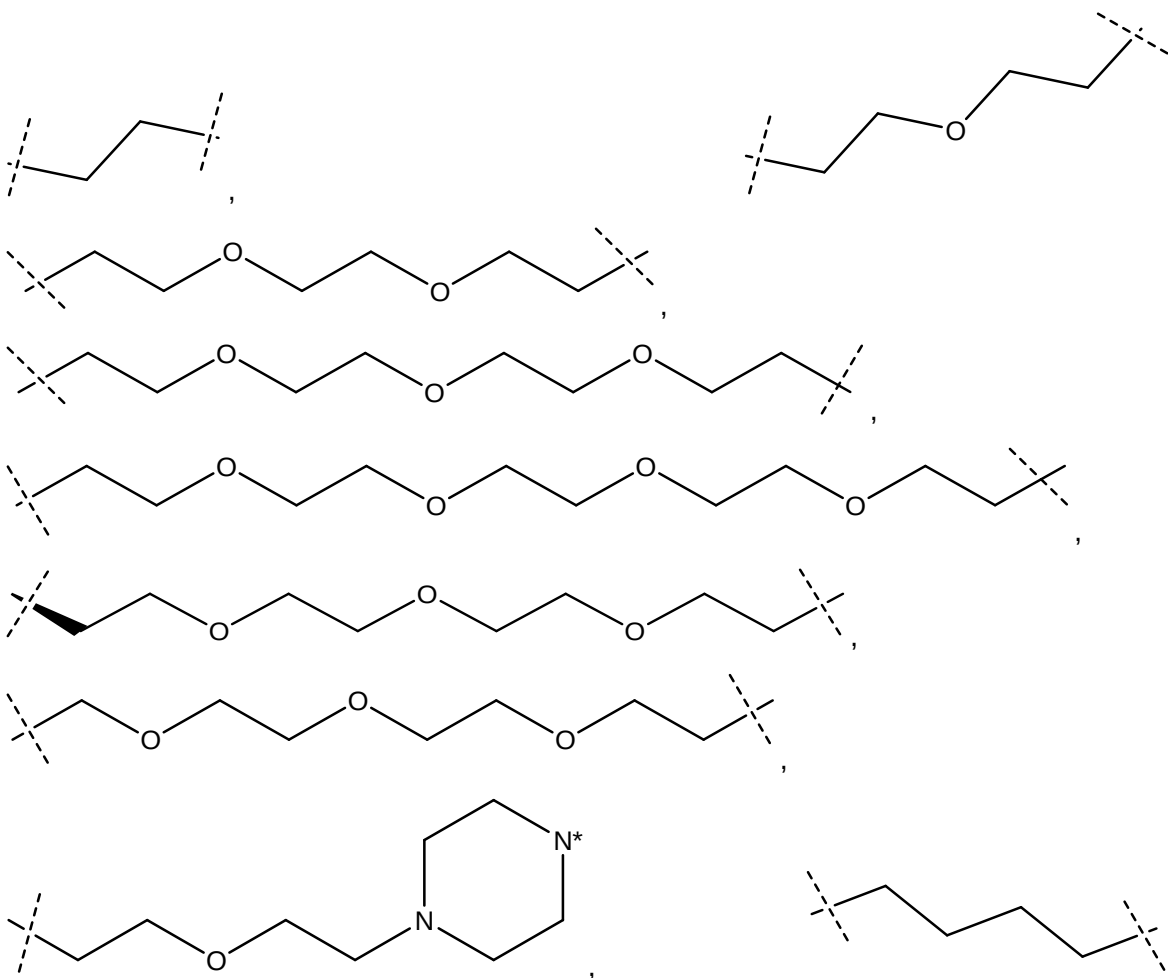


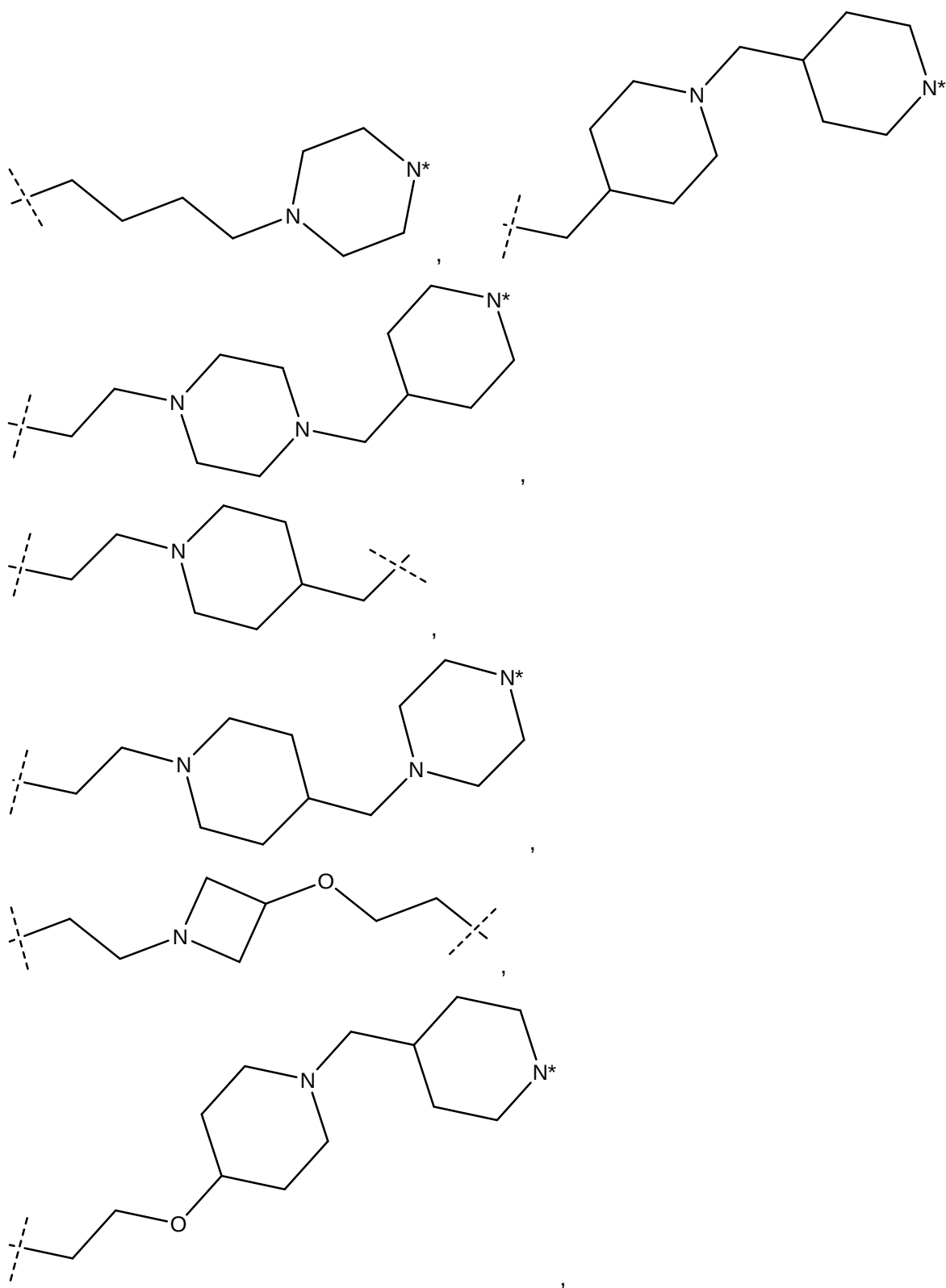


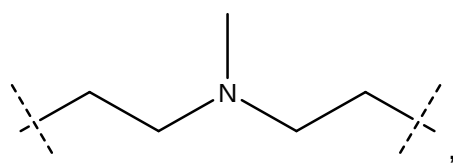
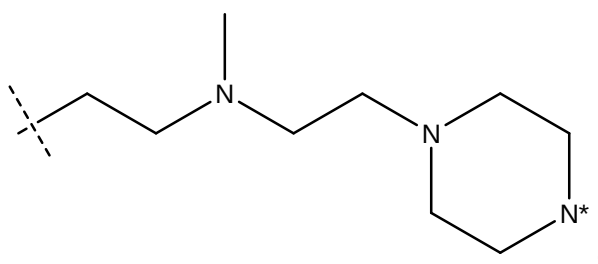
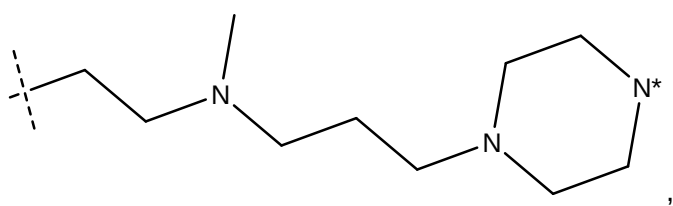
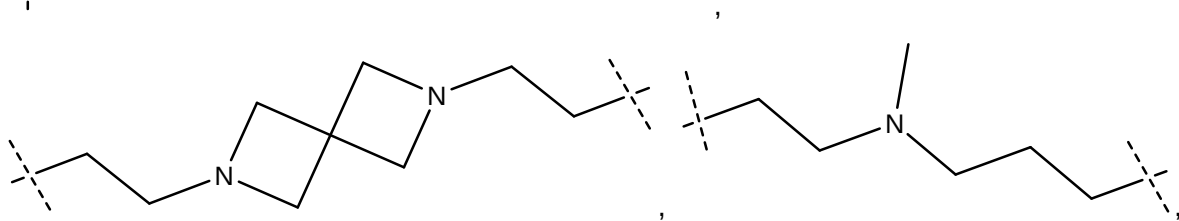
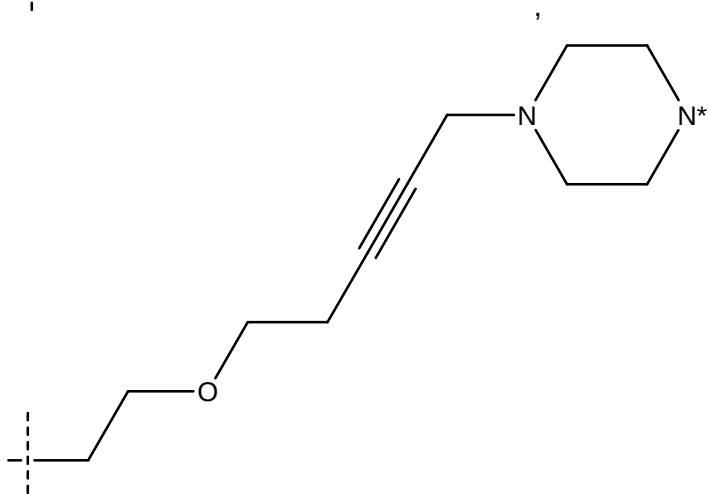
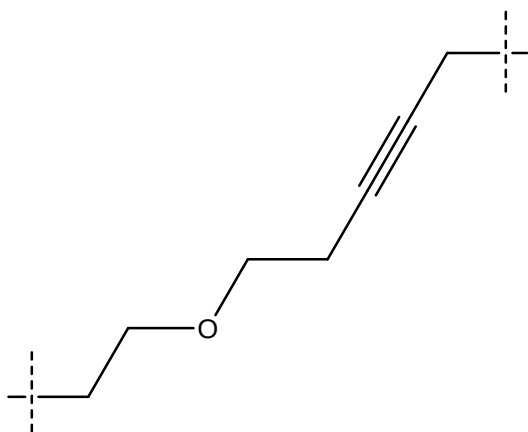


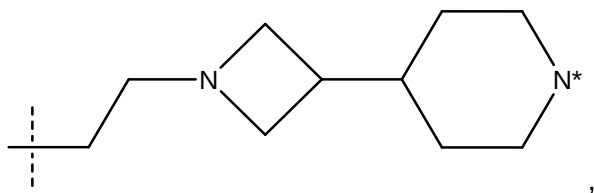
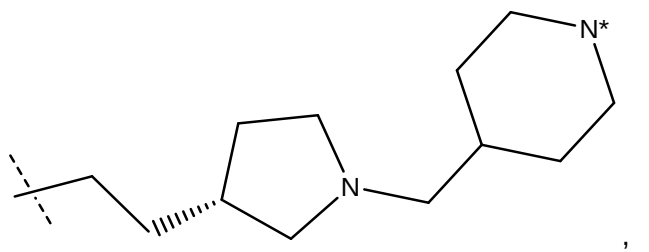
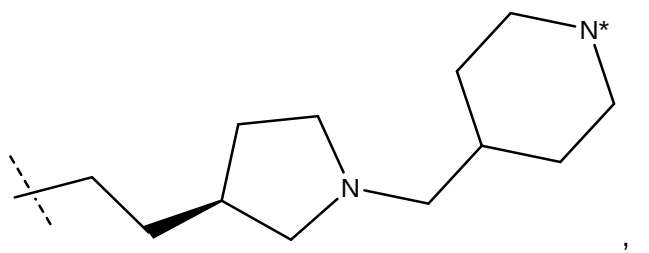
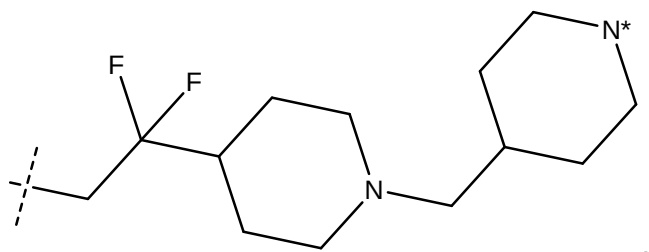
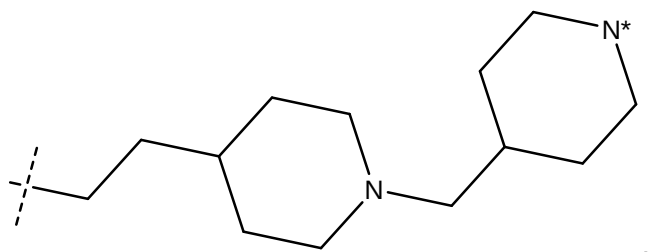
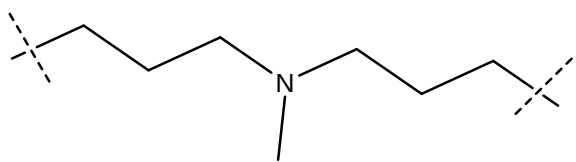
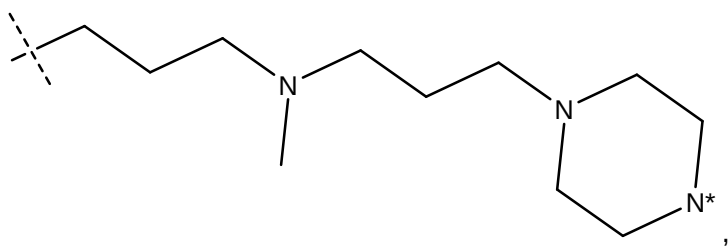
, en donde la PTM está unida covalentemente a la L a través de un átomo de heterocicloalquilo A o un sustituyente de este;

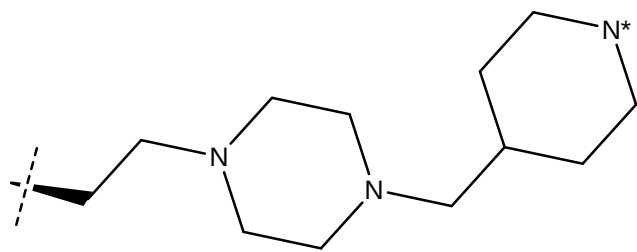
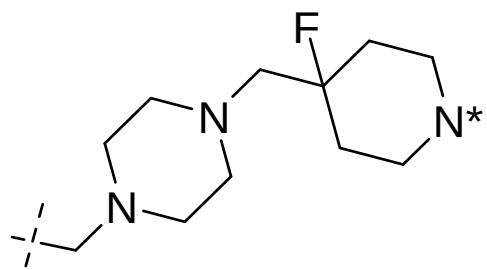
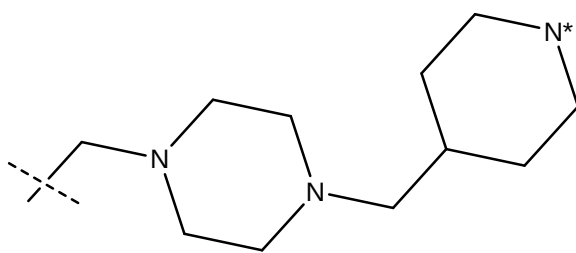
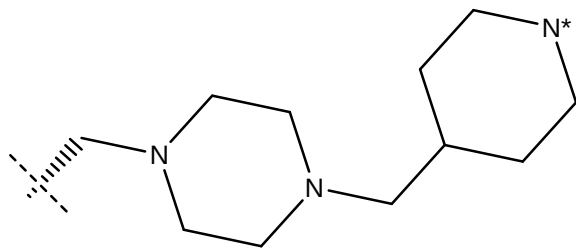
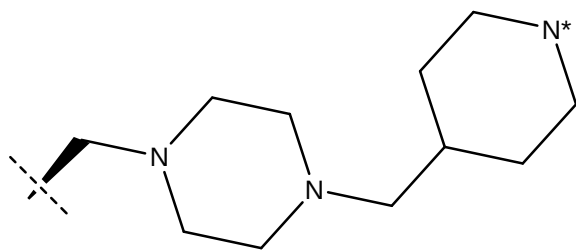
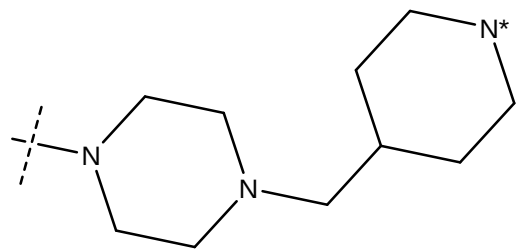
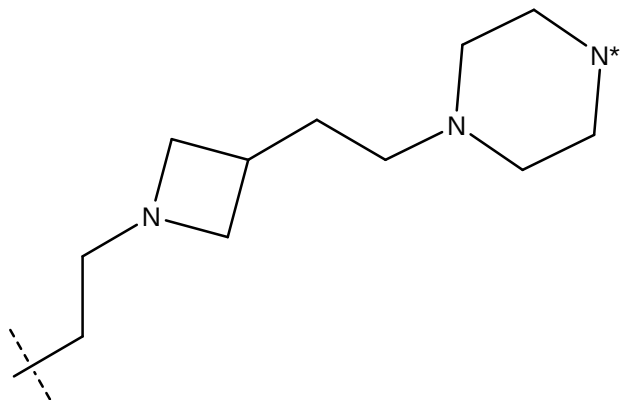
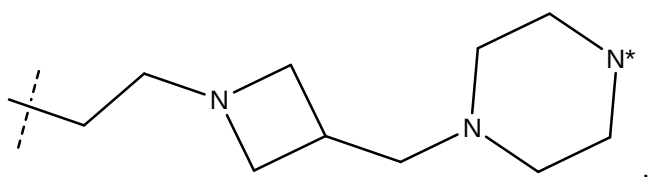
(c) L es un grupo enlazador (L) que se selecciona de:

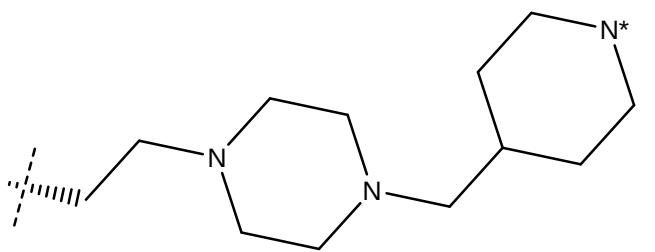




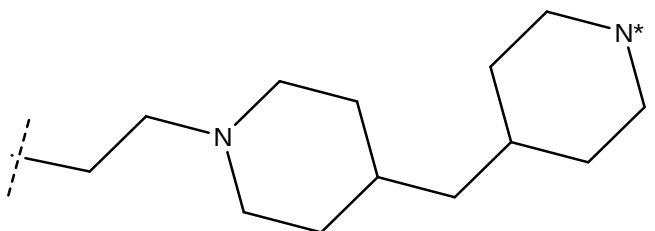




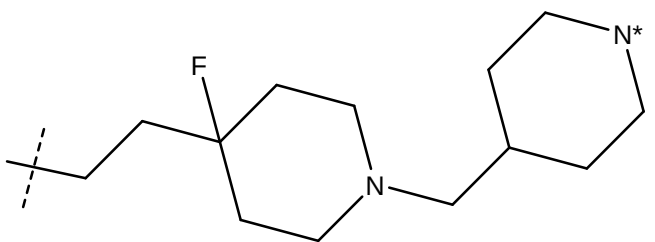




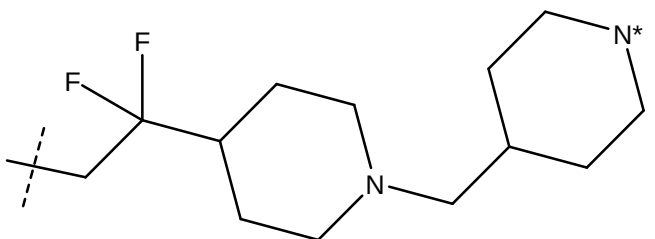
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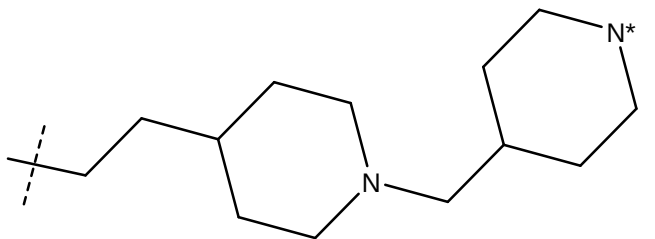
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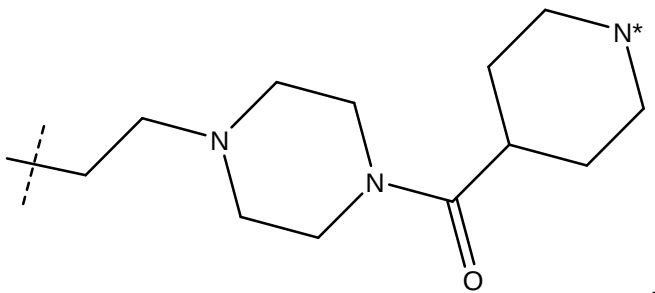
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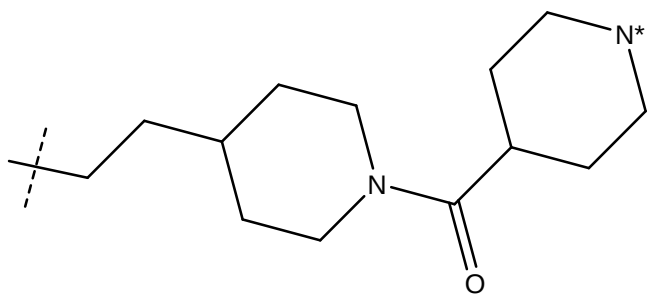
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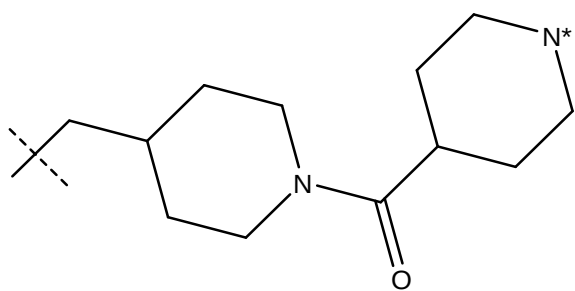
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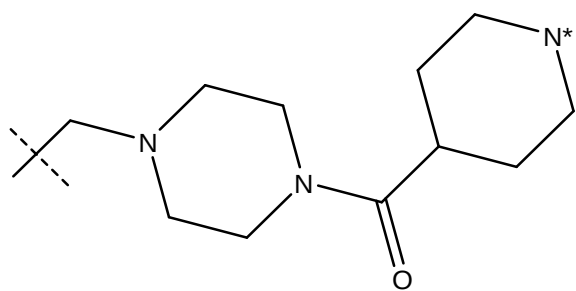
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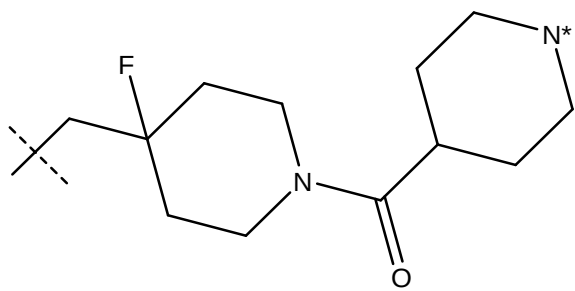
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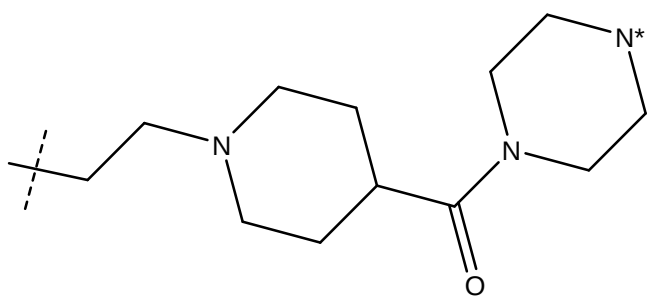
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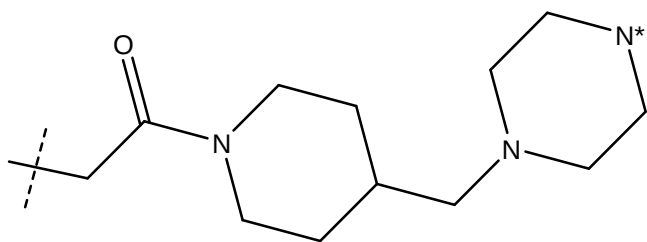
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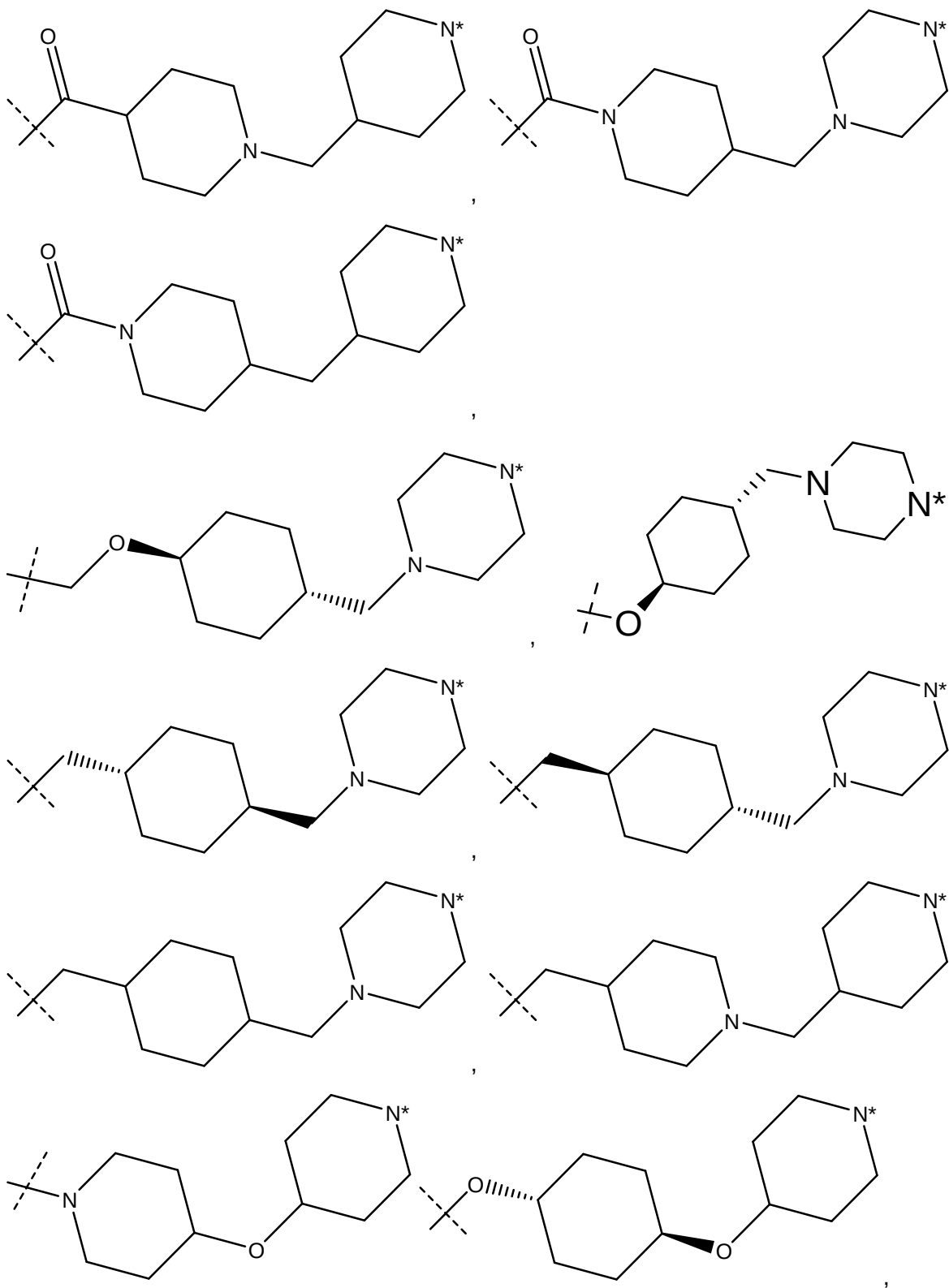
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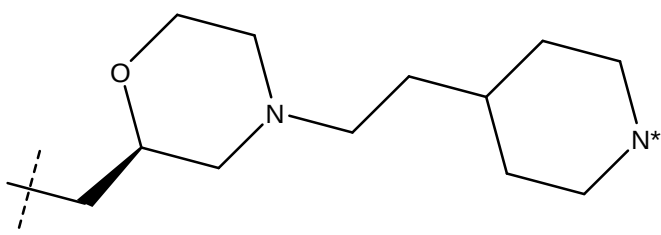
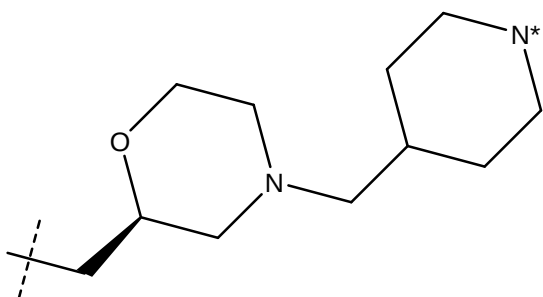
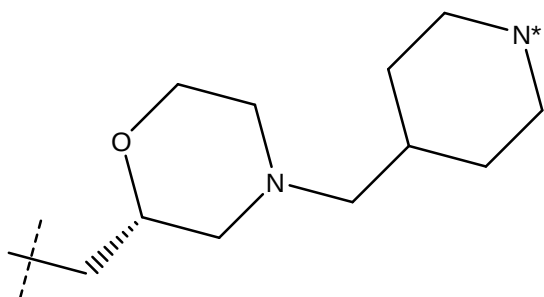
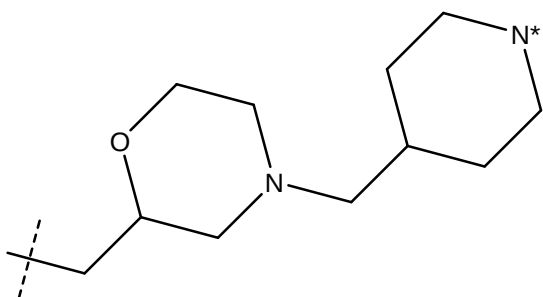
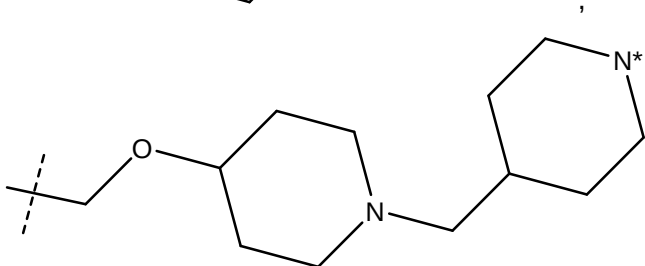
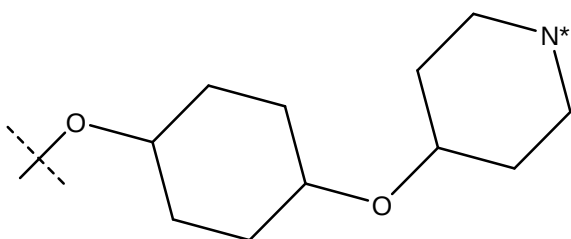
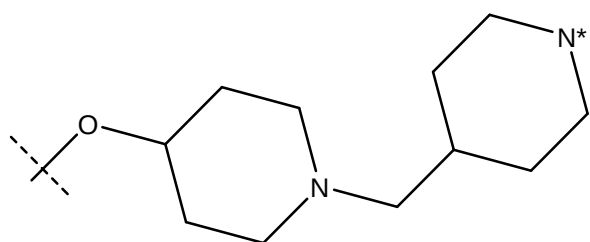
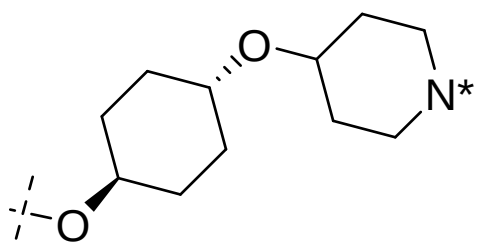


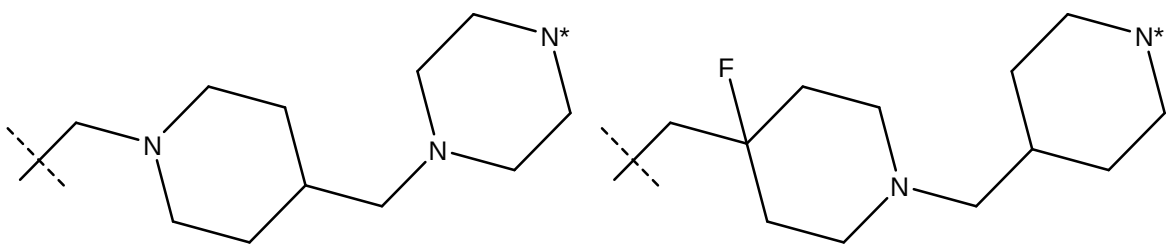
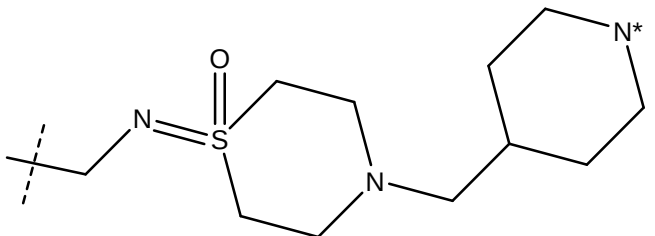
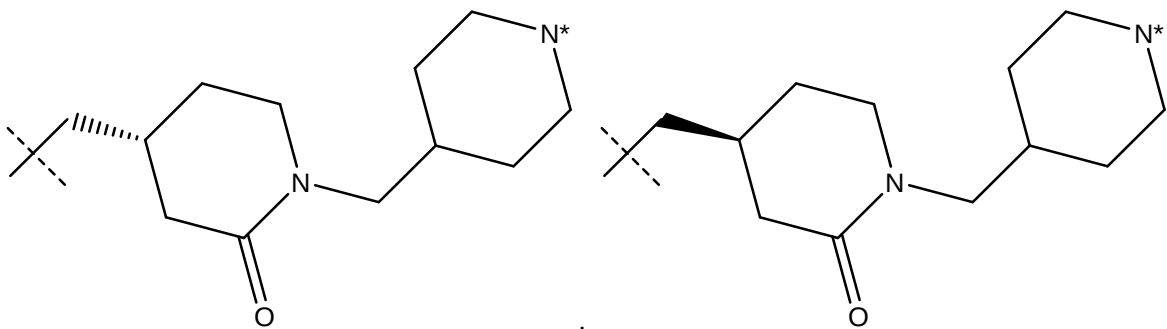
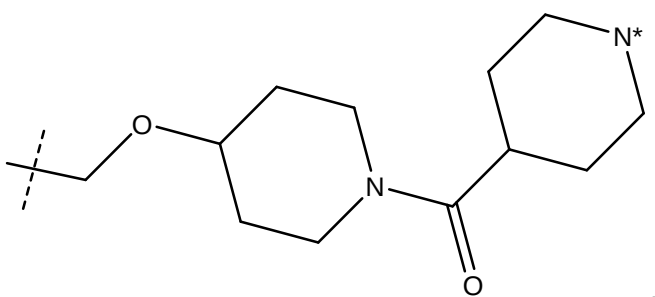
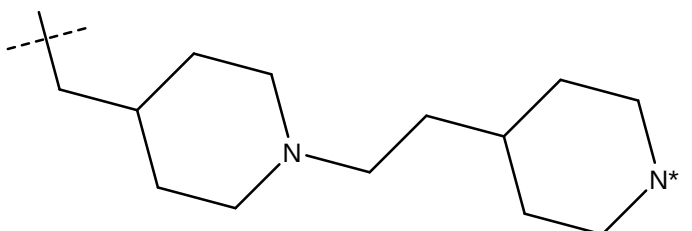
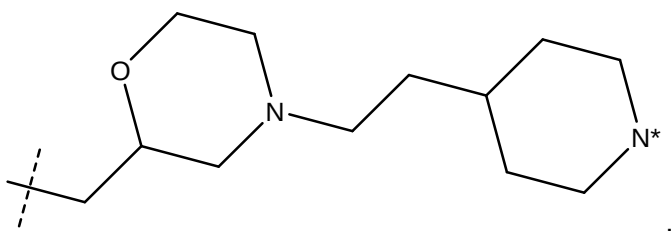
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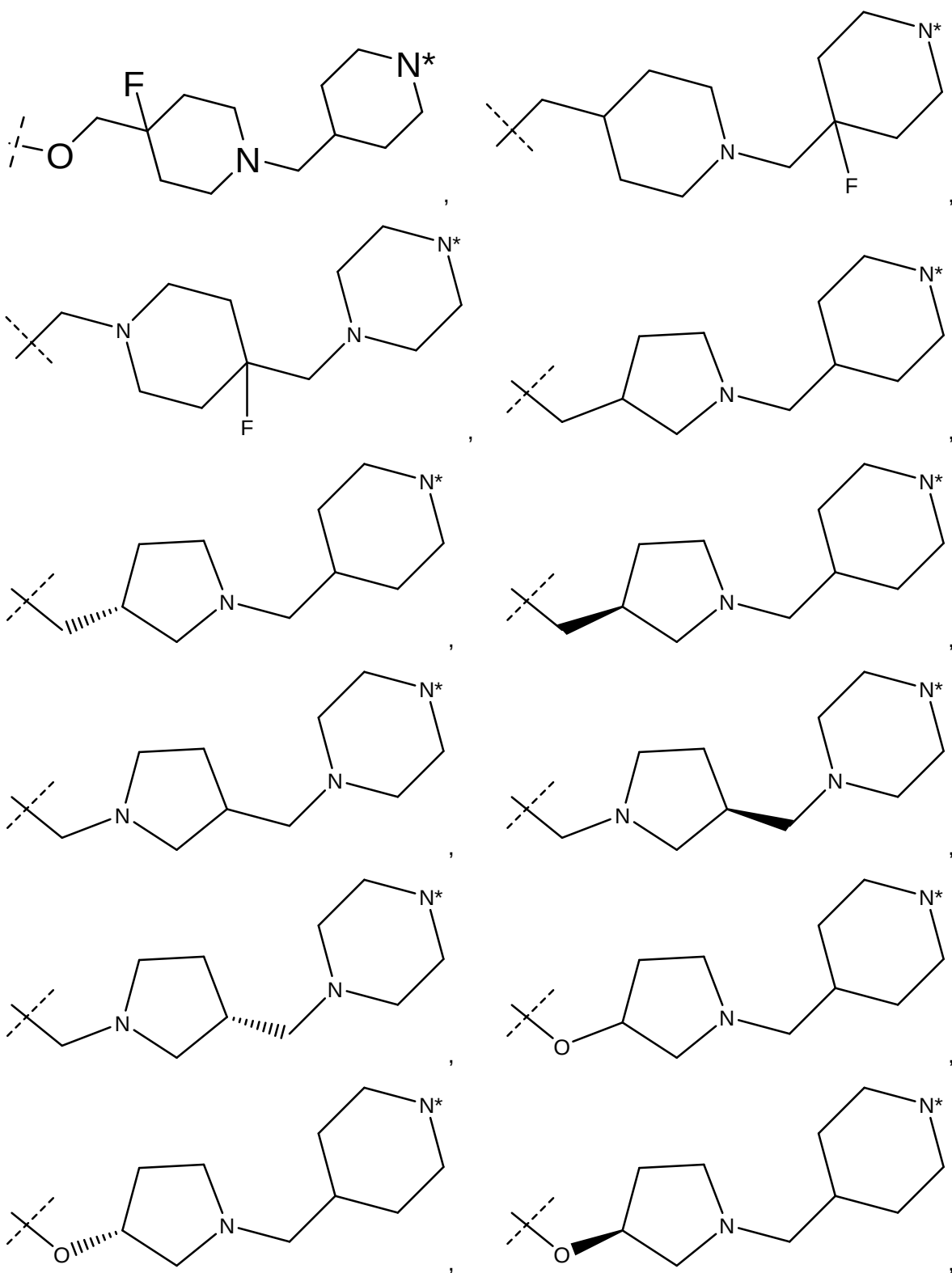


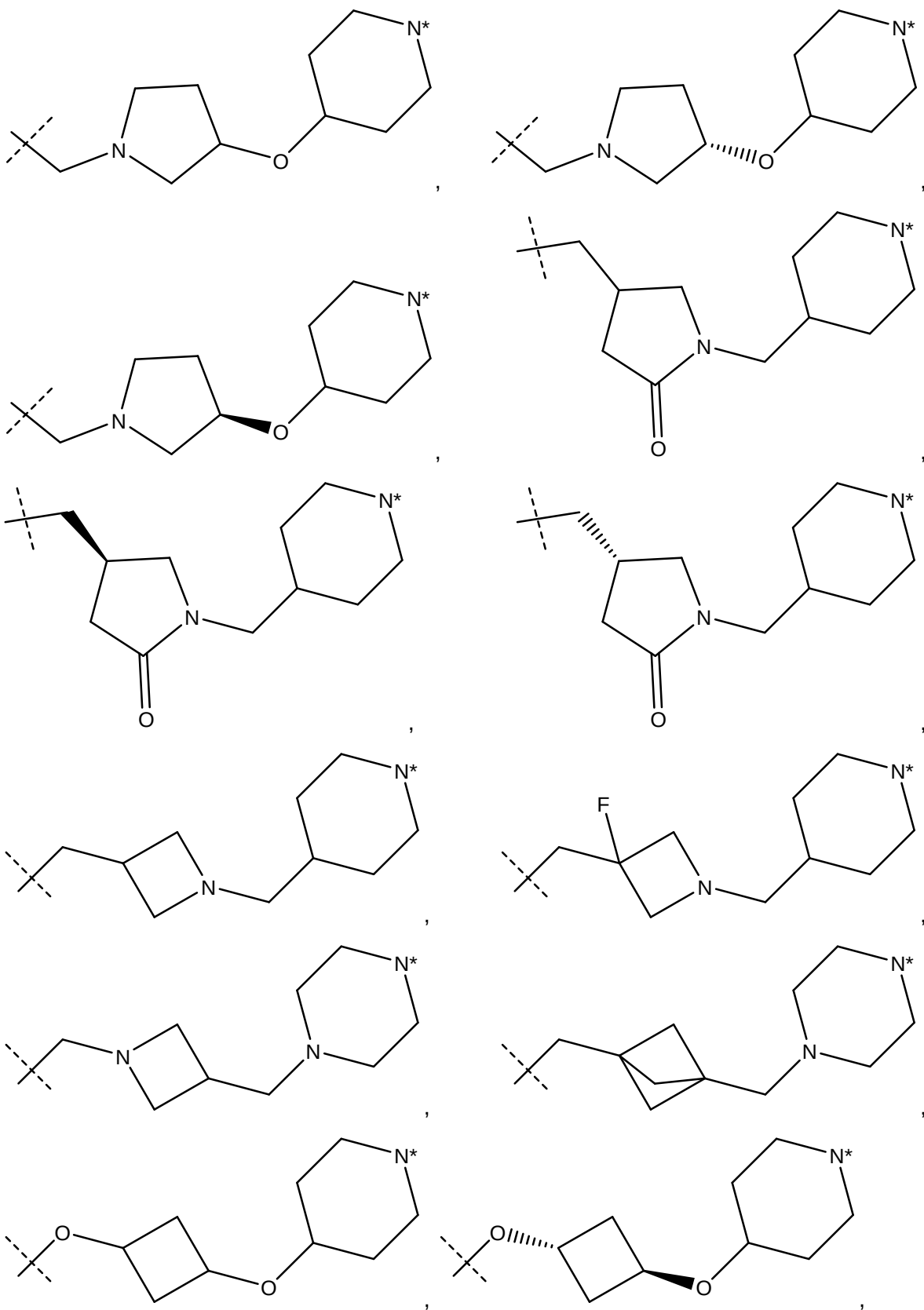
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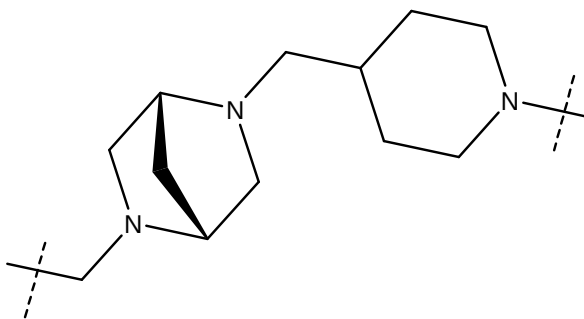
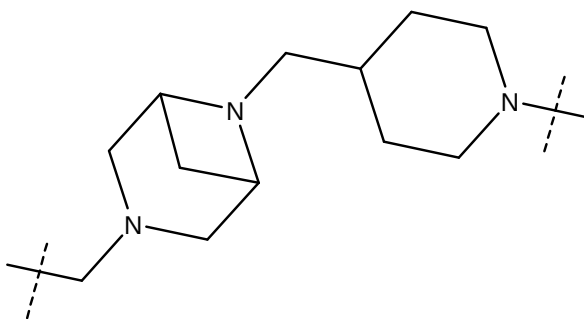
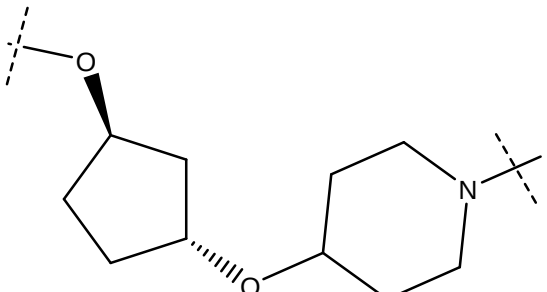
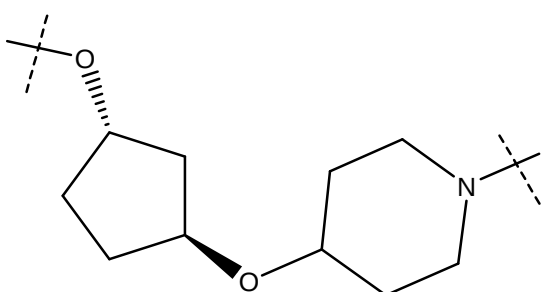
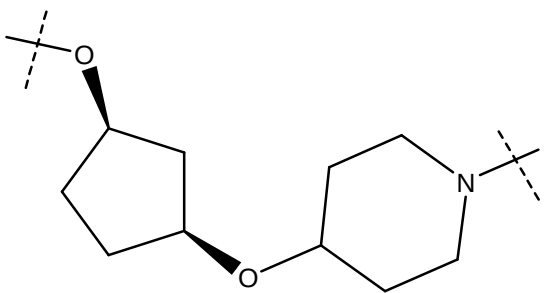
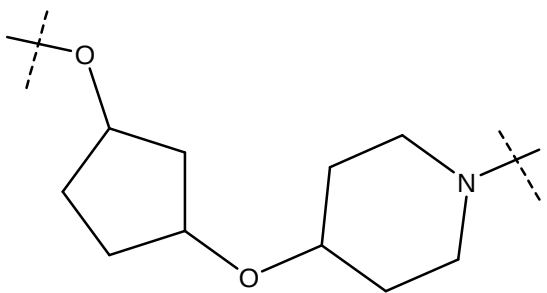
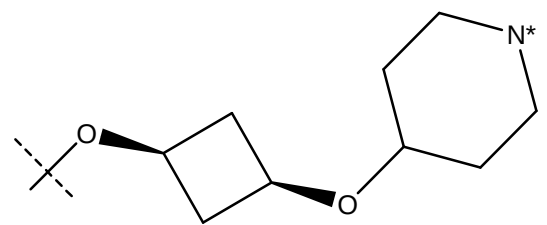
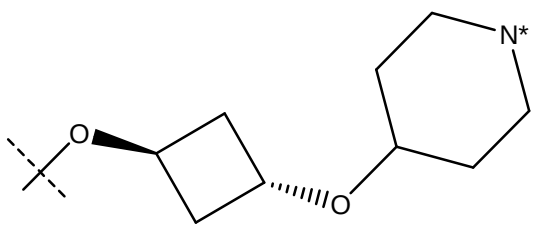


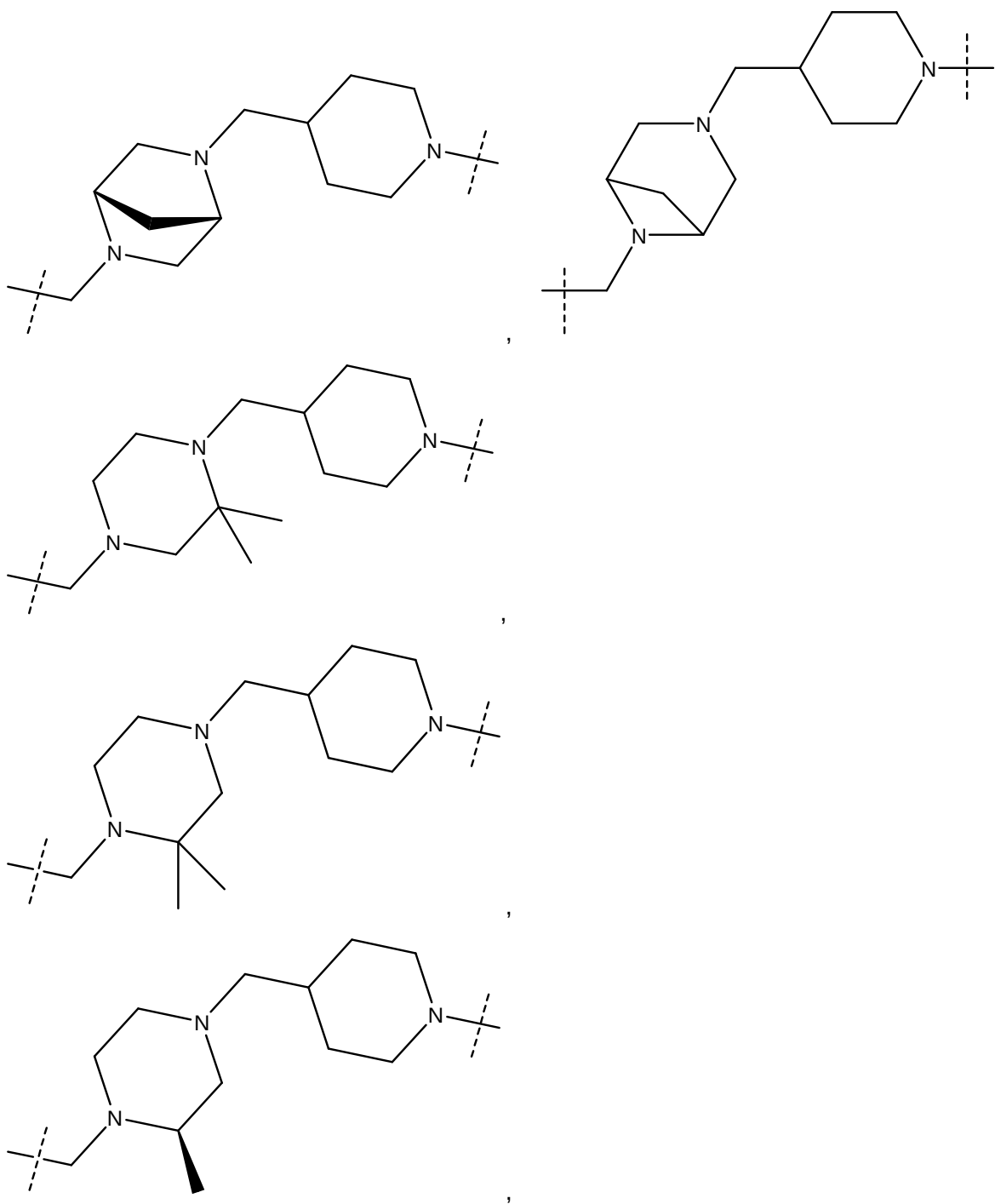


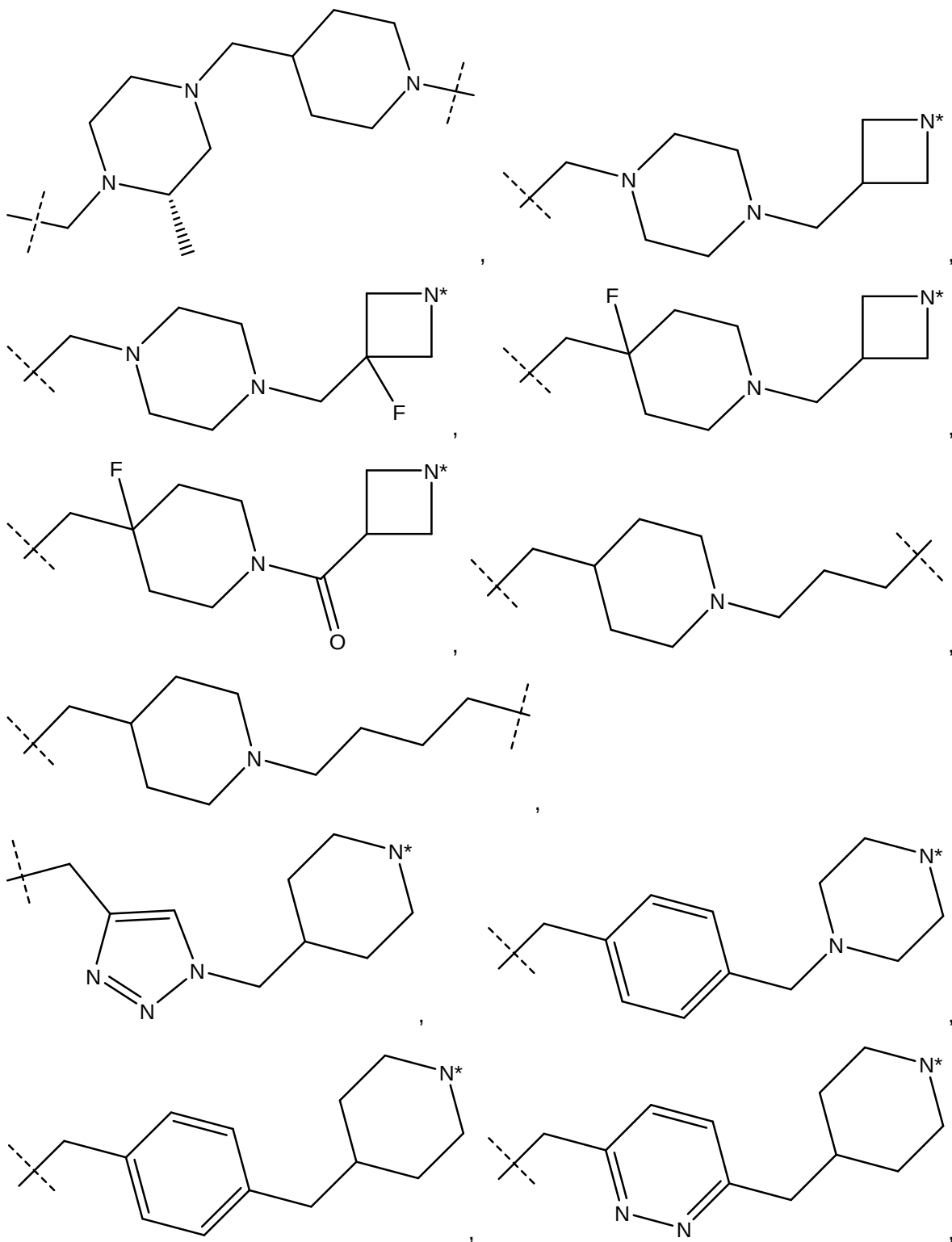


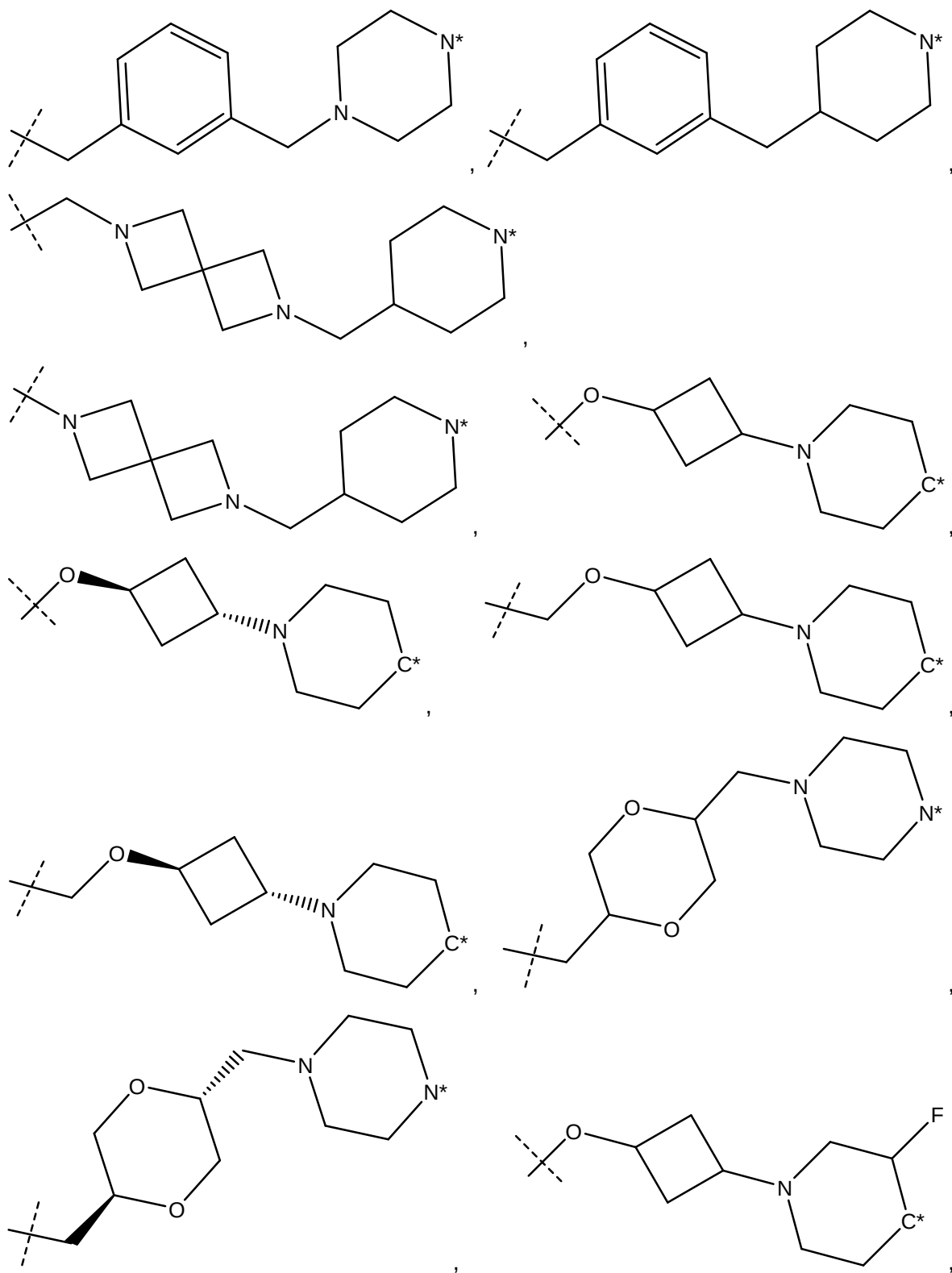


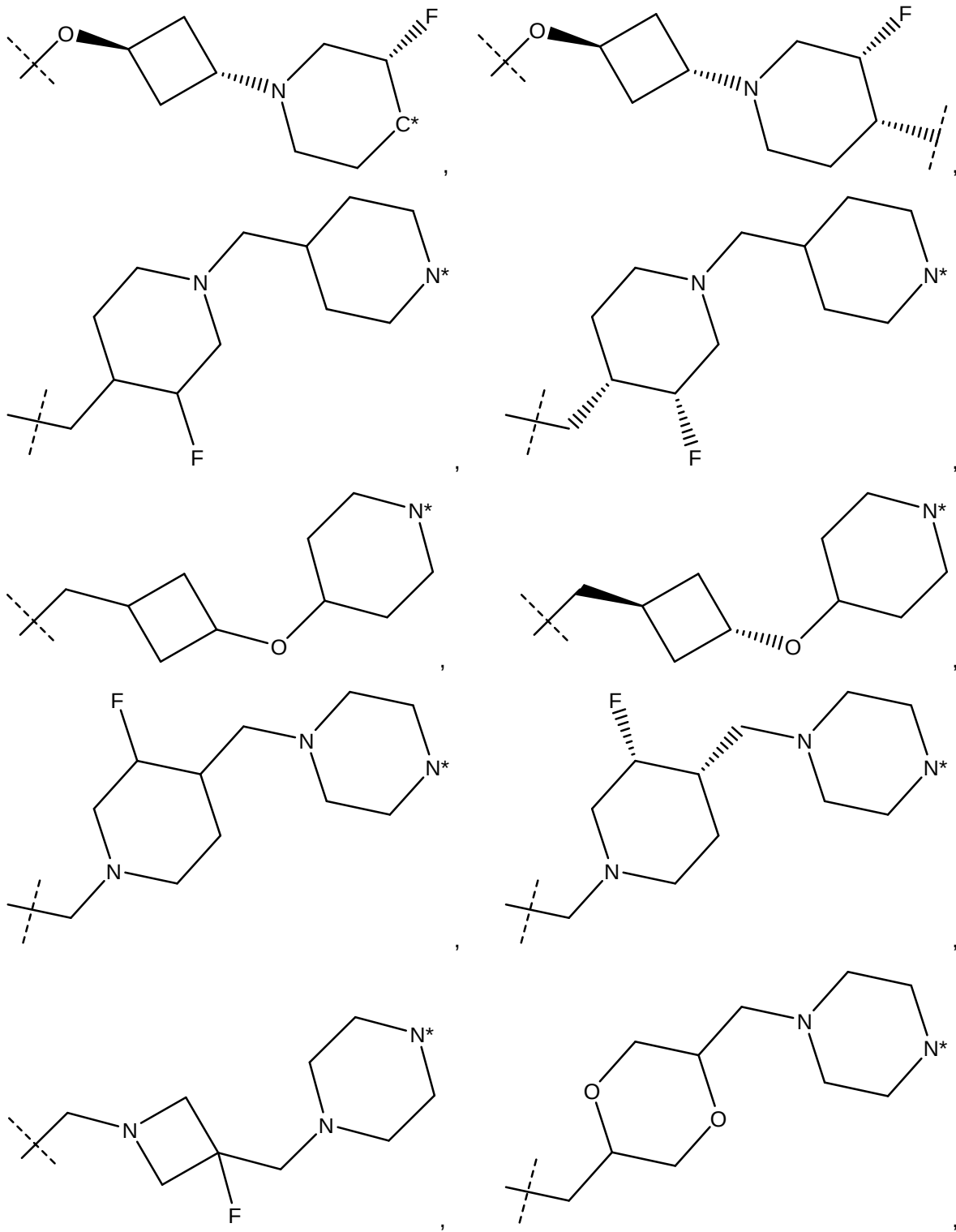


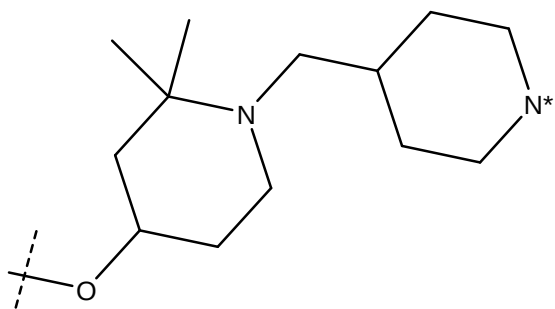
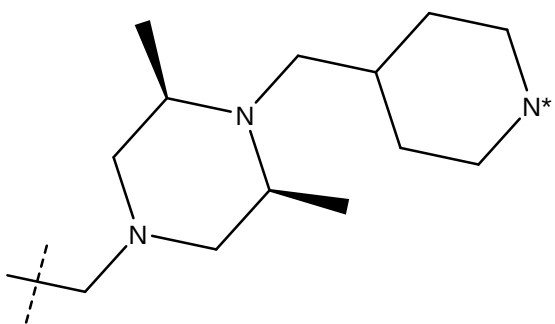
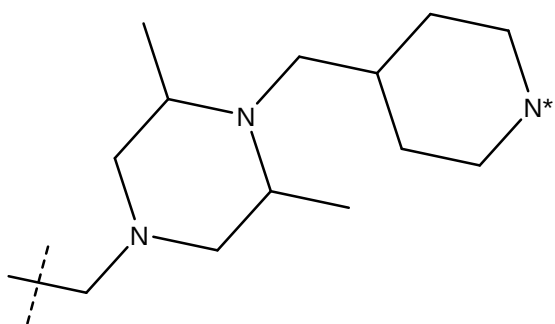
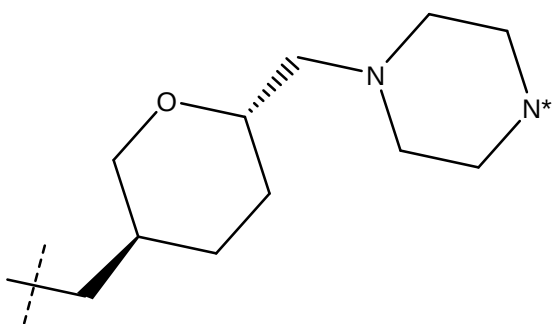
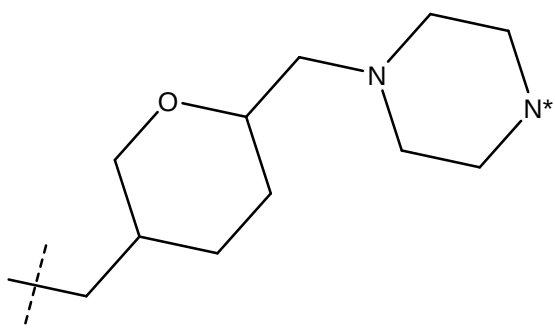
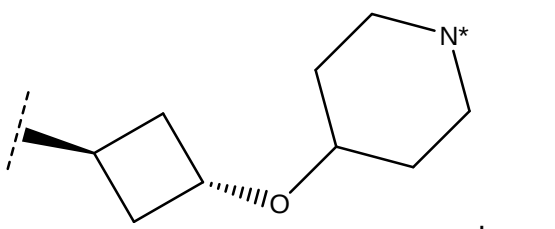
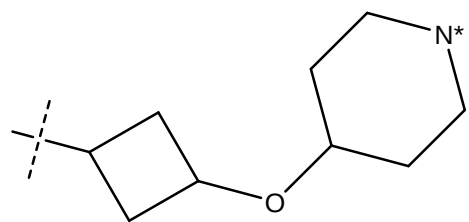
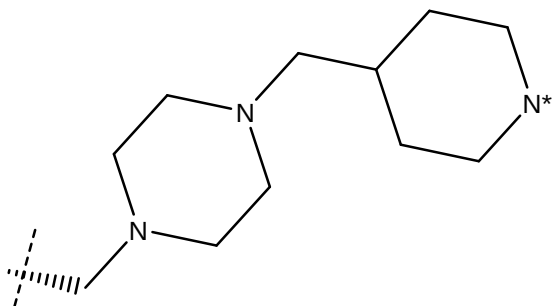
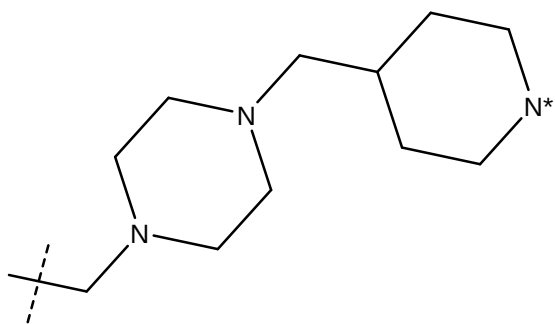
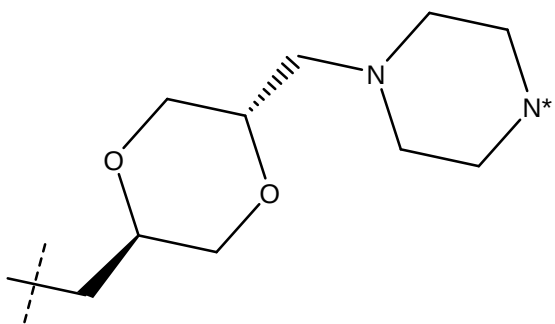


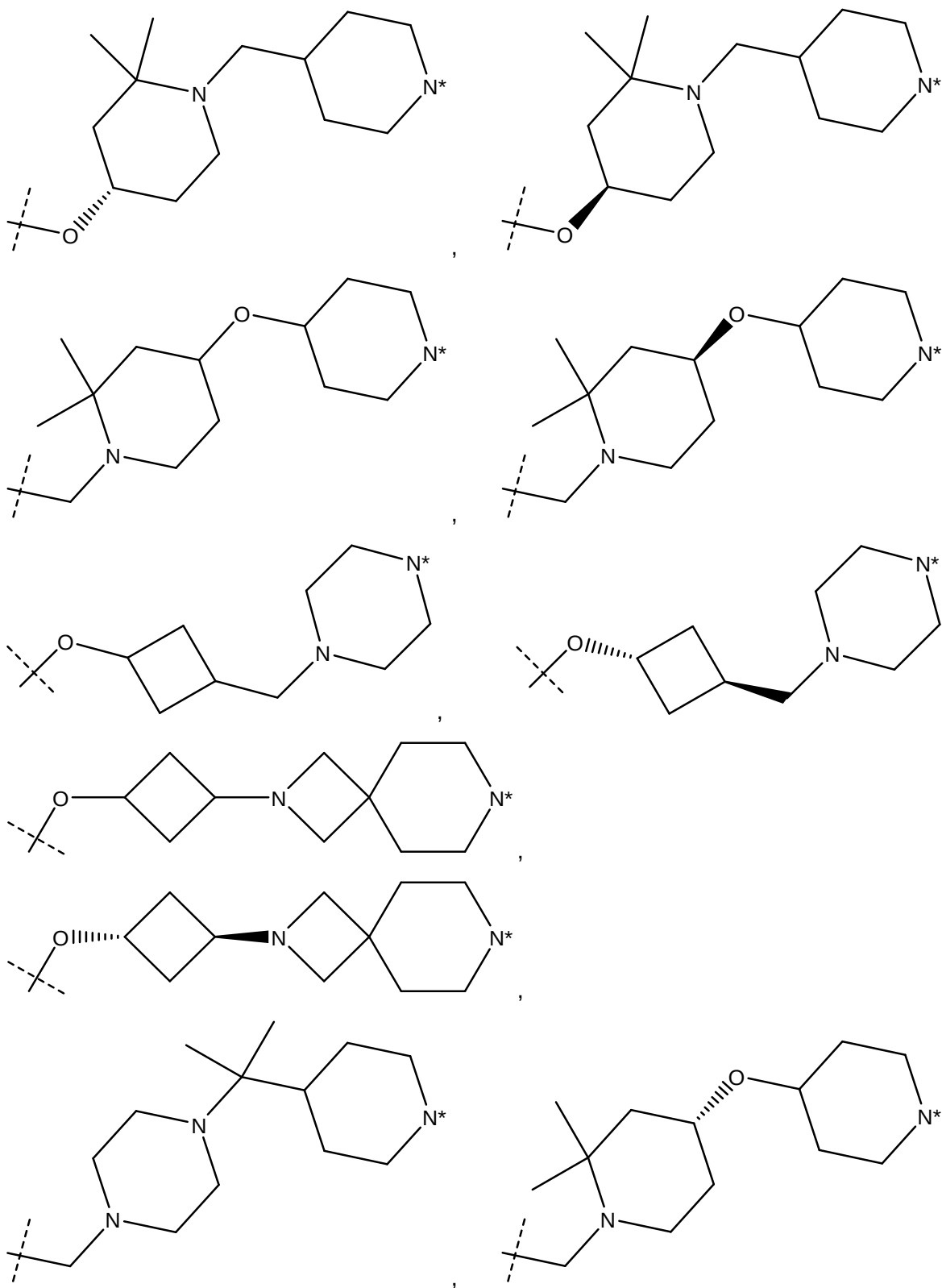


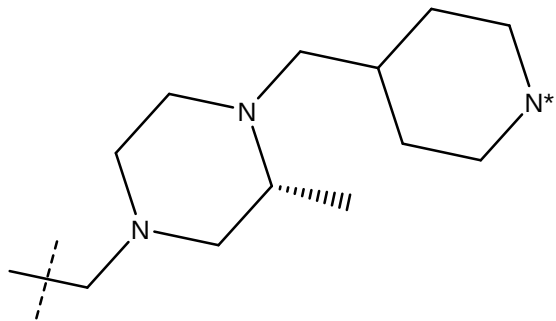
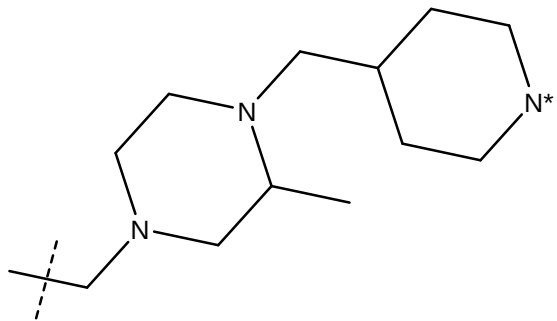
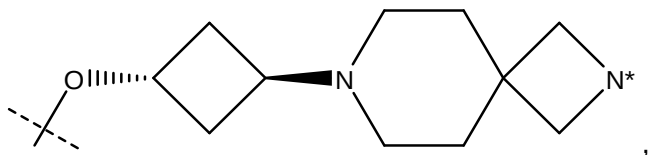
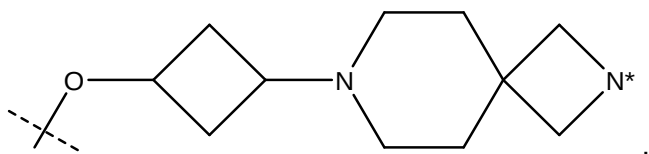
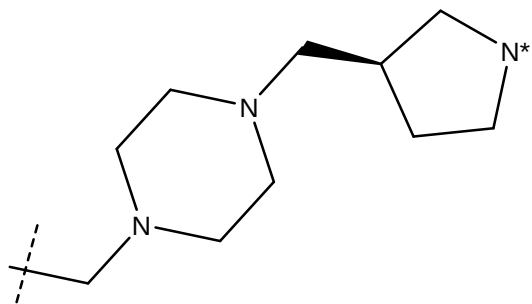
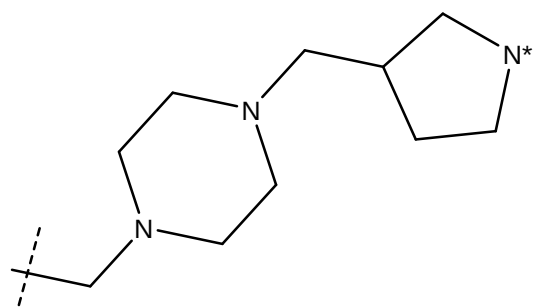
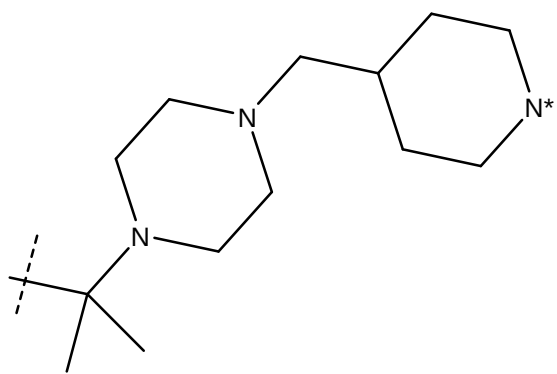
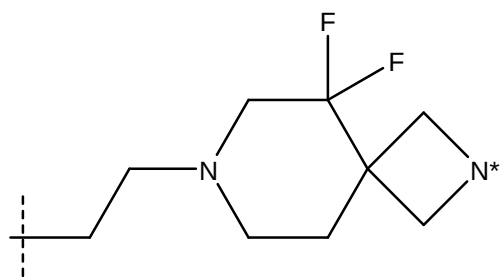
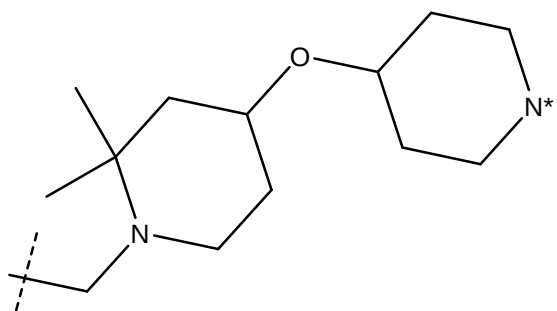


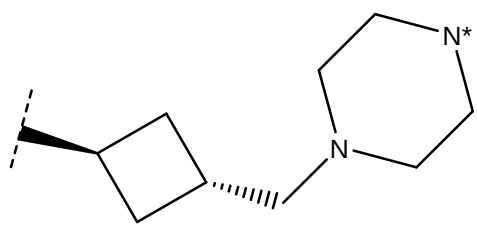
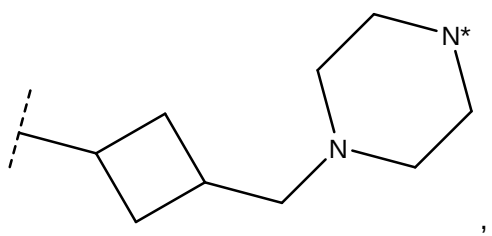
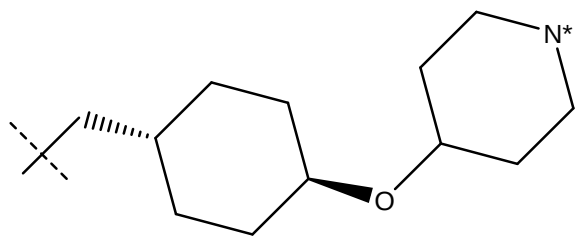
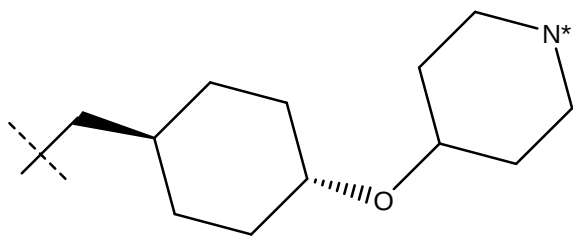
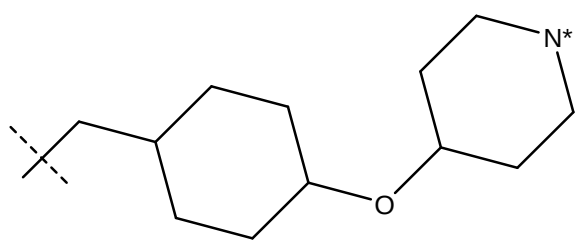
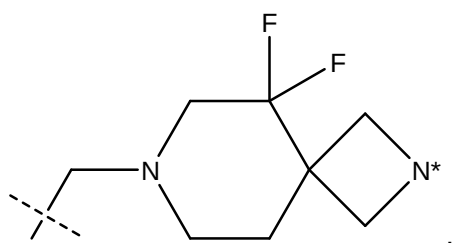
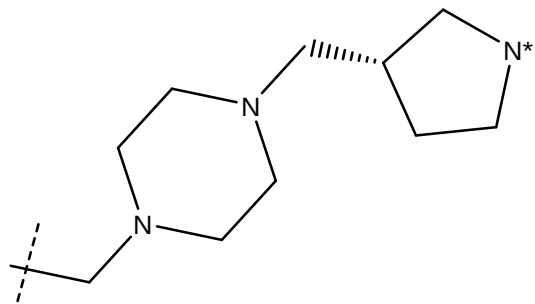
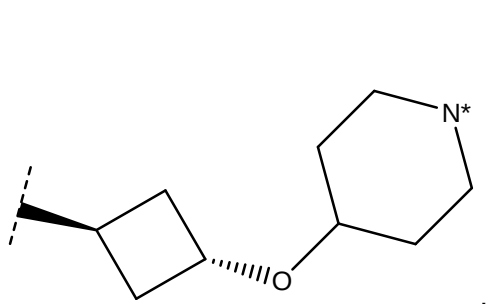
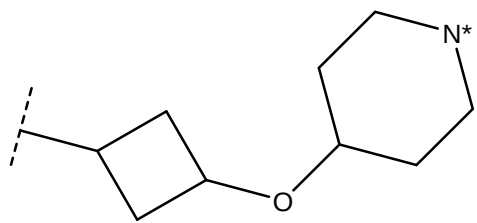
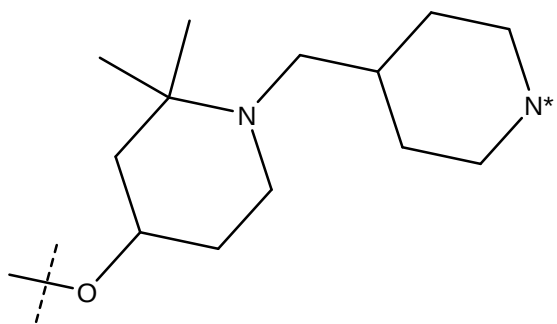


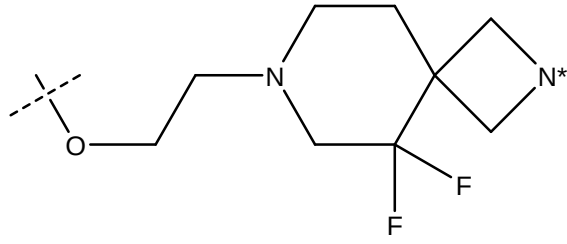
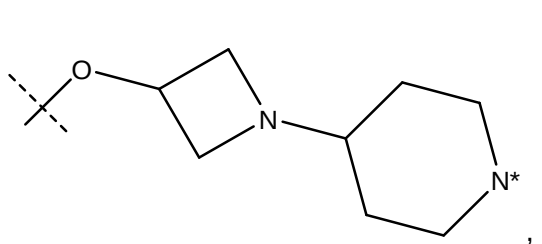
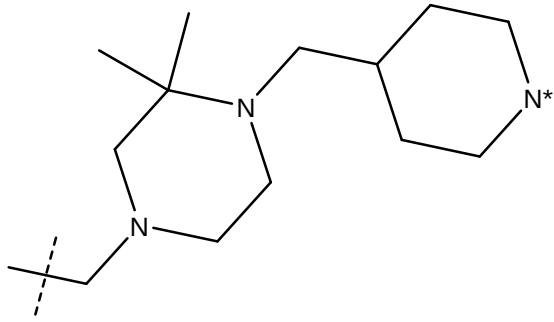
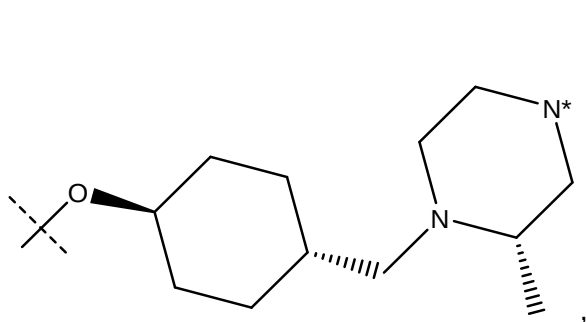
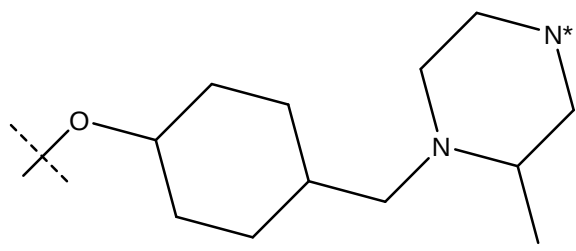
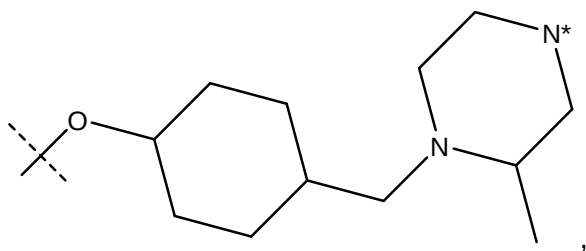
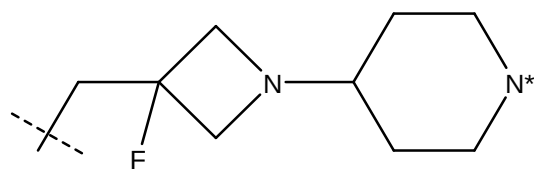
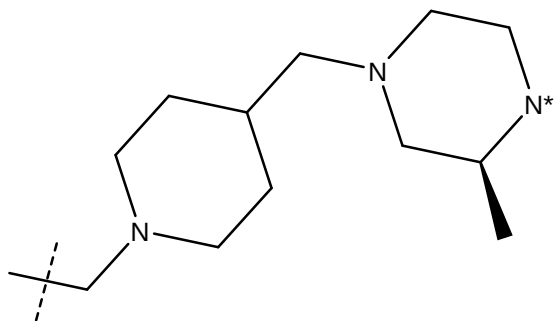
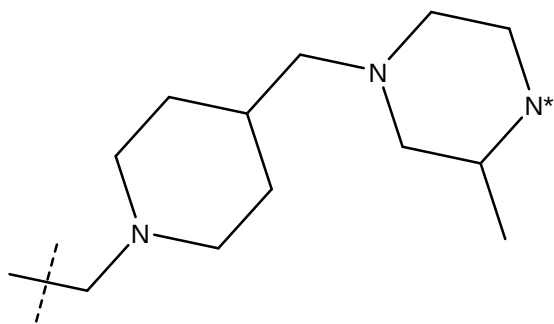
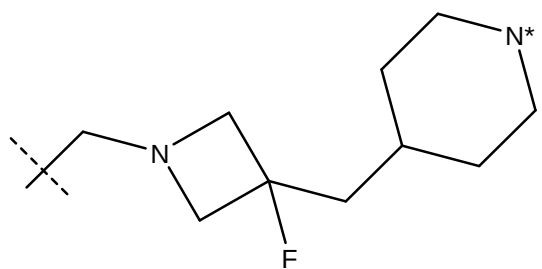


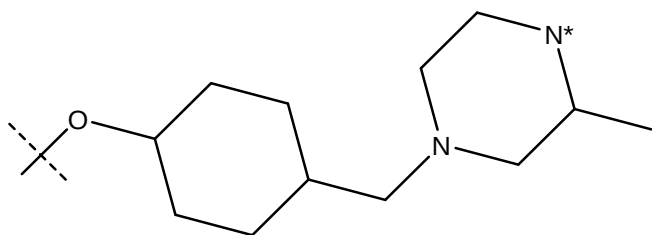




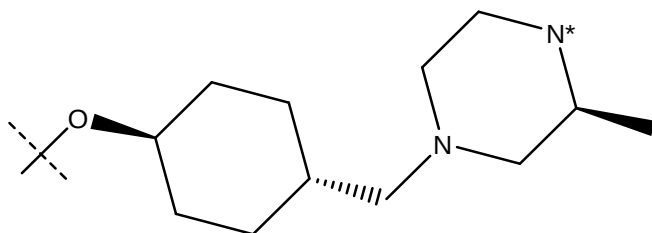




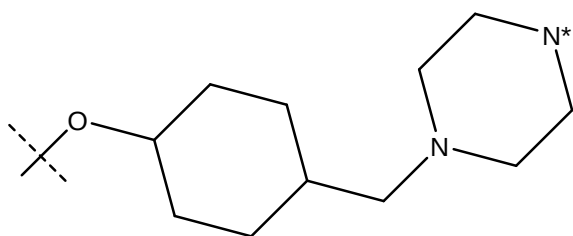




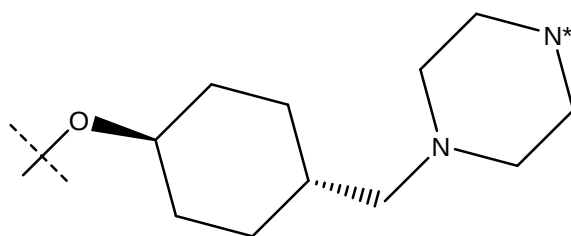
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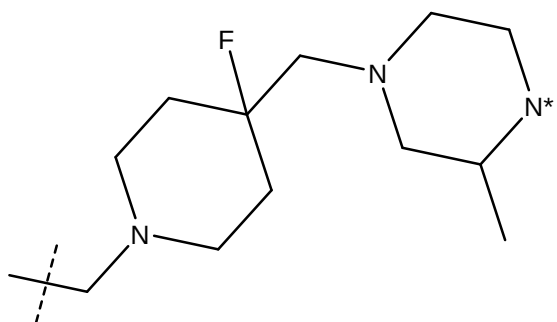
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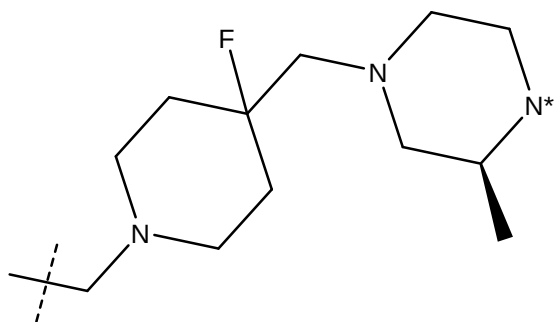
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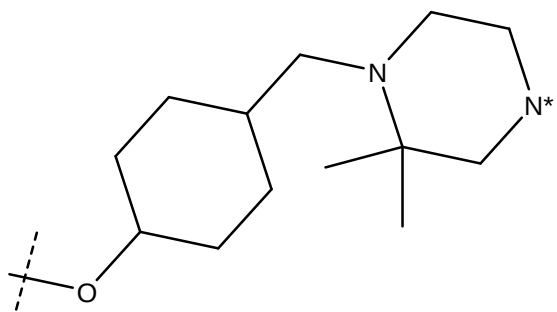
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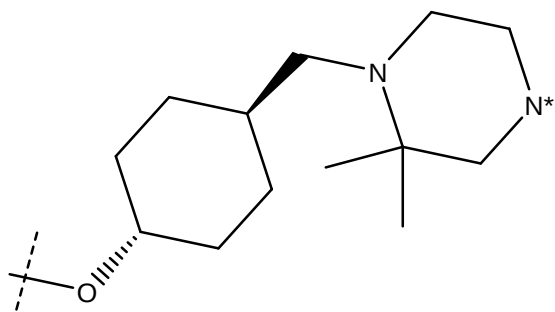
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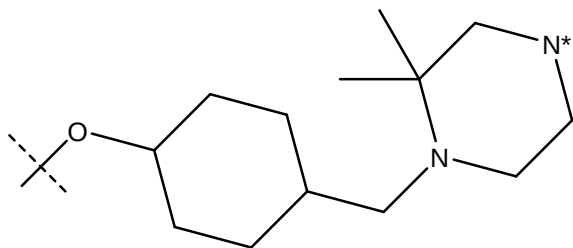
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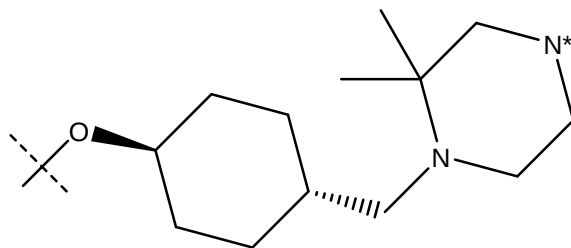
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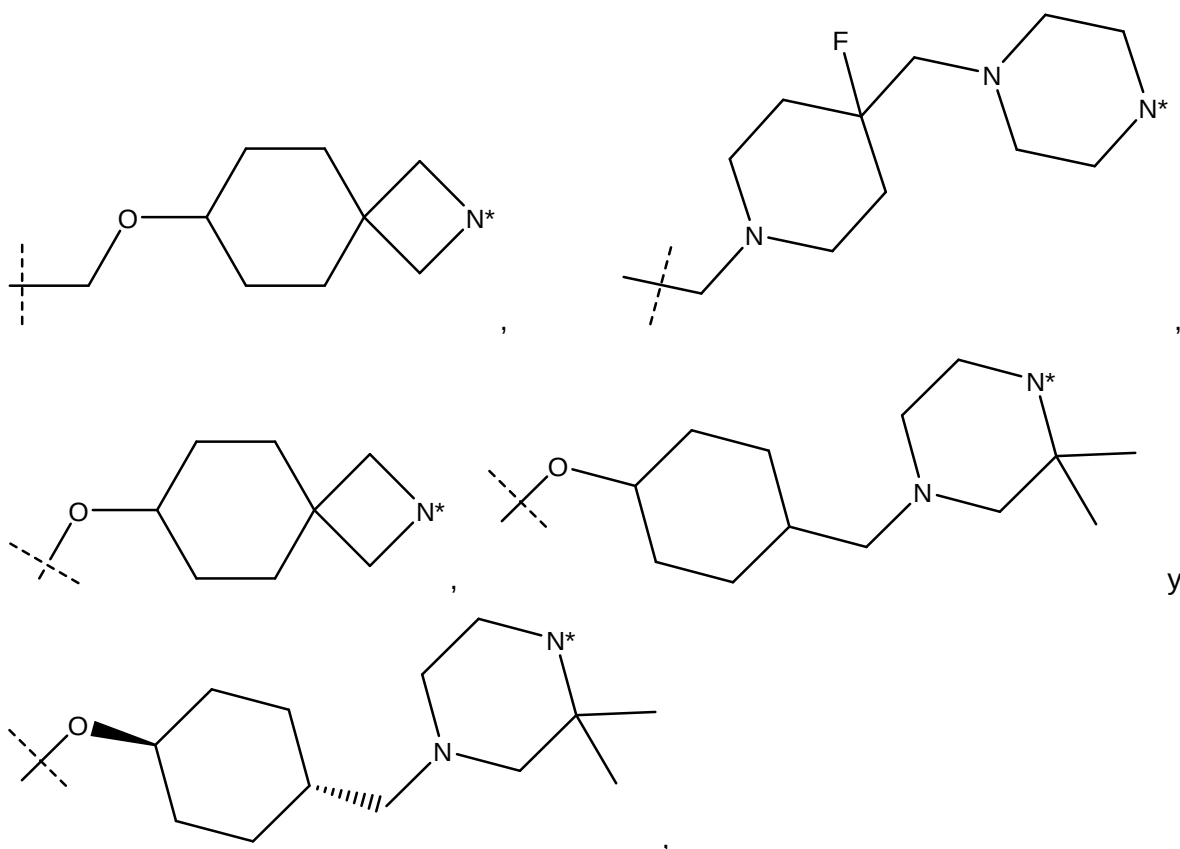
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en donde:

N* es un átomo de nitrógeno que está unido covalentemente o compartido con el CLM o el PTM;

C* es un átomo de carbono que está unido covalentemente o compartido con el CLM o el PTM; y

representaron el punto de unión al CLM o al PTM; o

(d) una combinación de estos.

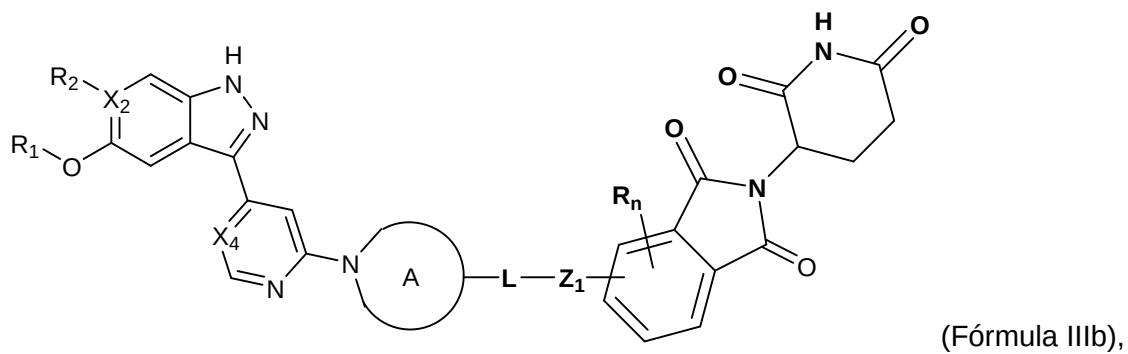
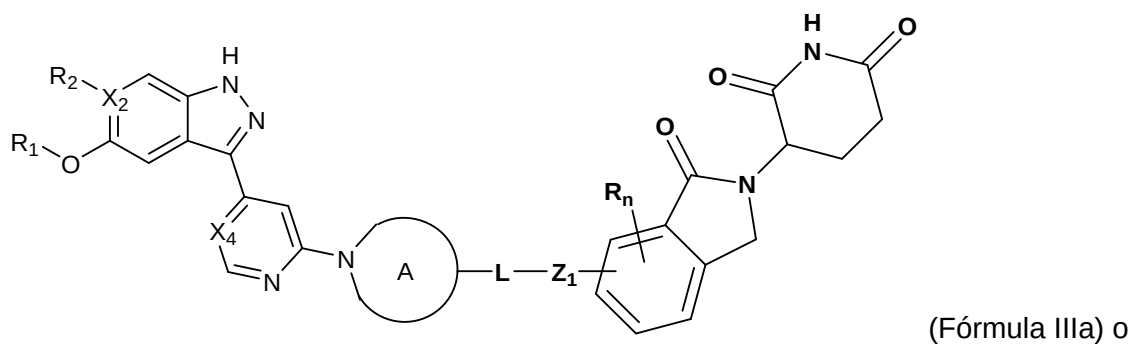
39. El compuesto de la reivindicación 1, en donde al menos uno de:

la PTM es una PTM que se selecciona de un compuesto de la Tabla 1;

la CLM es una CLM que se selecciona de un compuesto de la Tabla 1; y

la L es una L que se selecciona de un compuesto de la Tabla 1.

40. El compuesto de la reivindicación 1, en donde el compuesto está representado por la estructura química:



en donde:

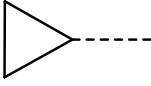
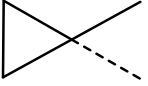
n es 0 o 1;

R es H, OH, -Cl, -F o Br;

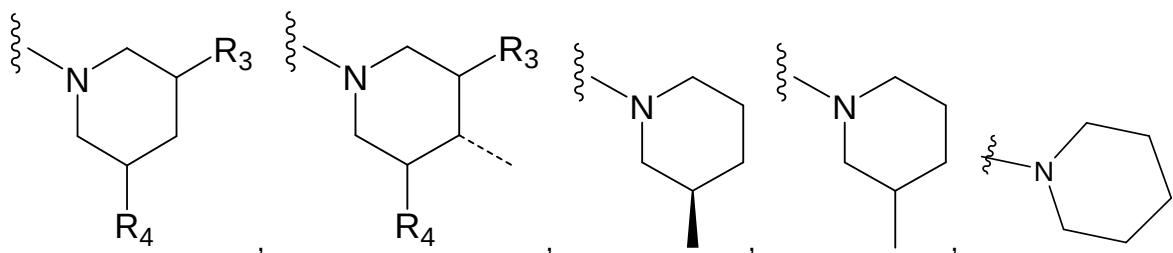
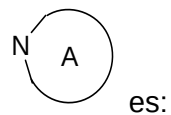
Z₁ es un nitrógeno o carbono compartido con un grupo cíclico de L;

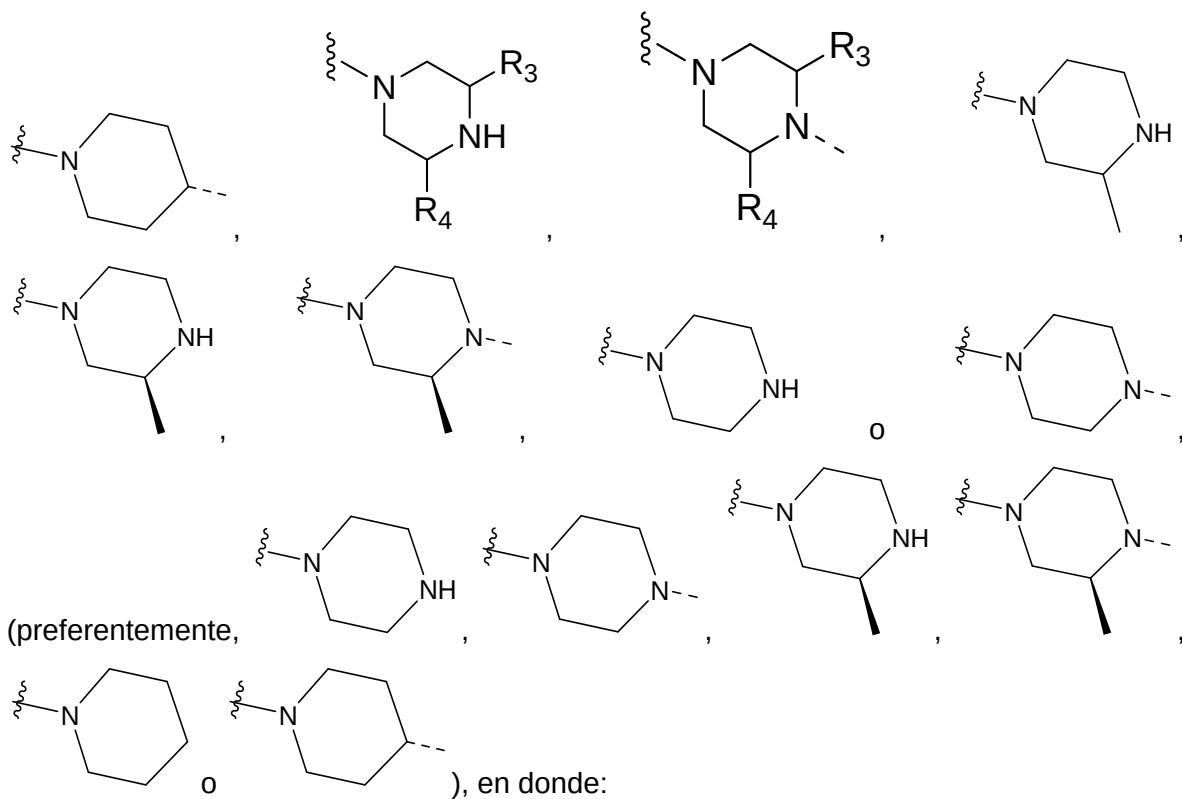
X₂ es C o N;

X₄ es CH o N (preferentemente N);

R₁ es  o  (preferiblemente ) , en donde  es el punto de unión al oxígeno de la PTM;

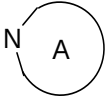
R₂ es un H, -Cl o -F;





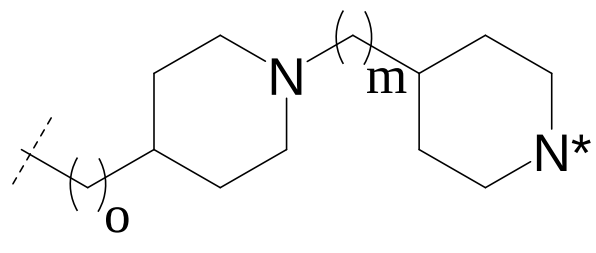
R_3 es H, metilo o etilo;

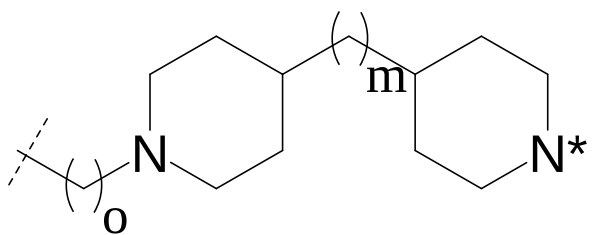
R_4 es H, metilo o etilo;

— indica el punto de unión del  al PTM; y

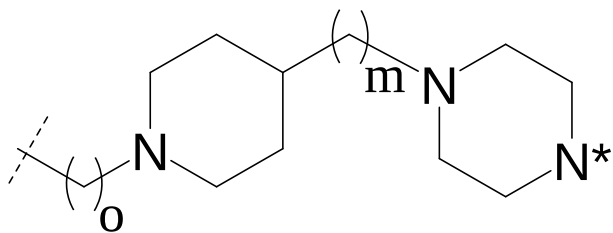
— indica el punto de unión de la PTM con la L, y cuando — no está presente, puede estar unida a la L a través de un átomo del grupo cíclico (por ejemplo, un carbono o nitrógeno);

L está representado por la estructura química:

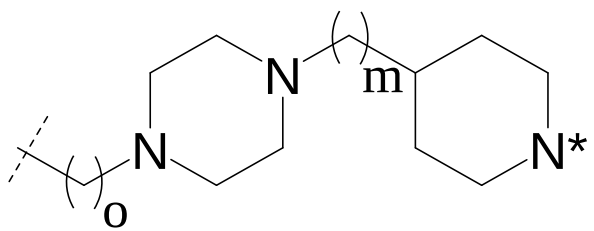




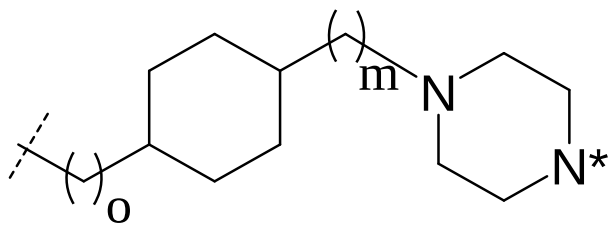
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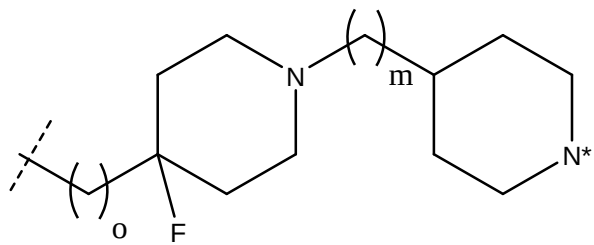
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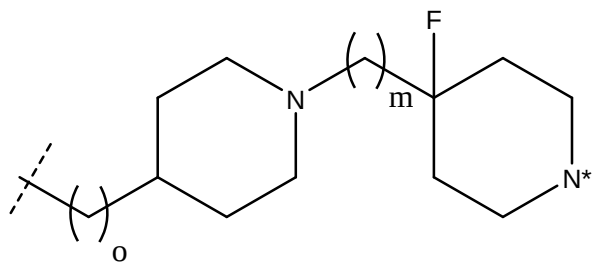
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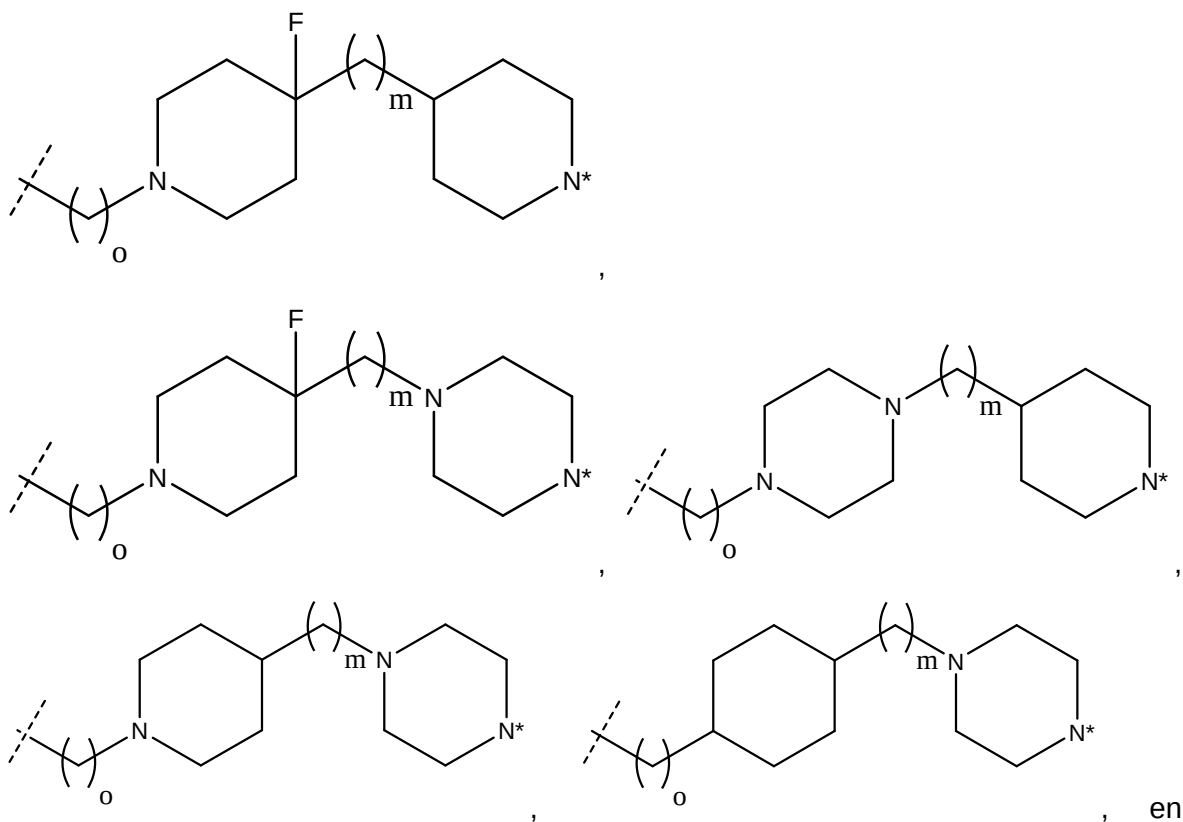
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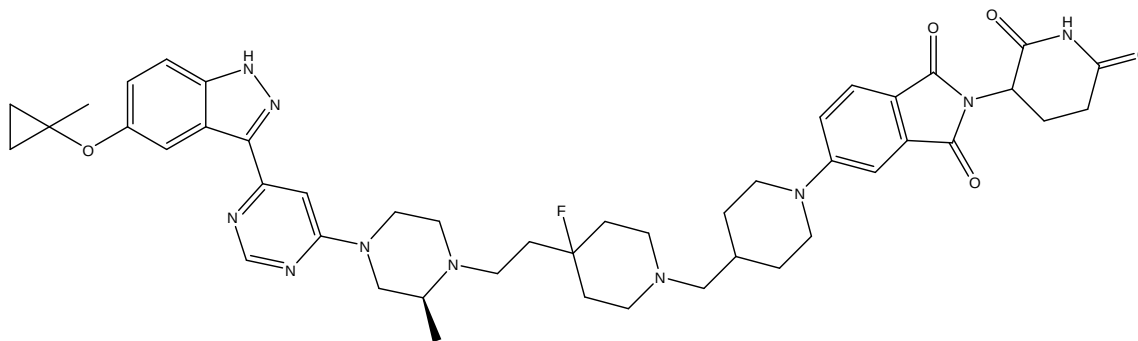
donde:

m y n son números enteros que se seleccionan independientemente de 0, 1, 2 o 3 (preferentemente 1); y

la L está opcionalmente sustituida con 0, 1, 2 o 3 (preferentemente 0 o 1) grupos que se seleccionan de: $-Cl$, $-F$ y alquilo C_{1-3} (por ejemplo, metilo o etilo).

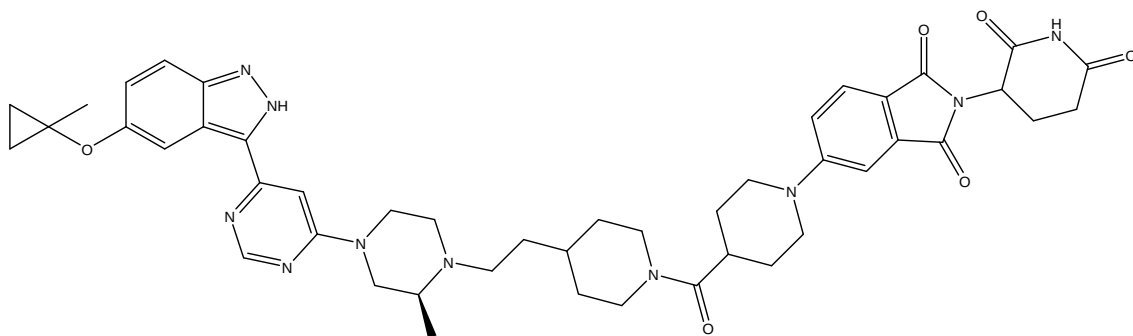
41. El compuesto de la reivindicación 40, en donde X_2 es C y X_4 es N.

42. El compuesto de la reivindicación 1, en donde el compuesto se selecciona del grupo que consiste en los compuestos 52-384 de la Tabla 1:

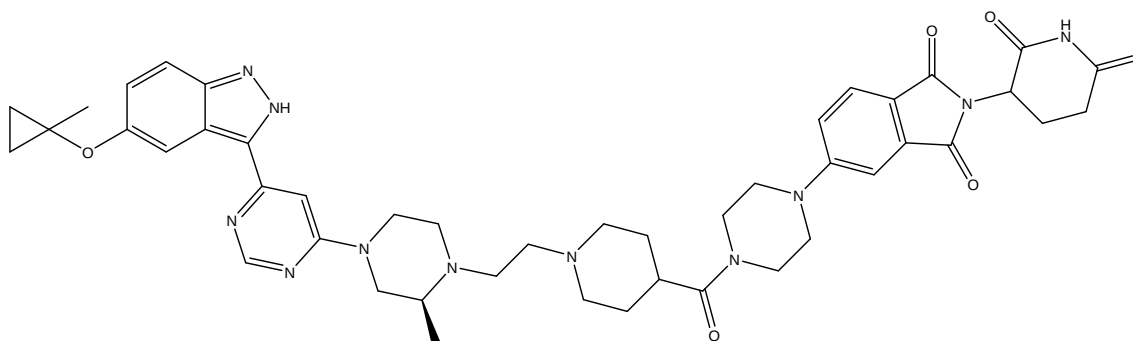


[illegible]CC1(CCN(C1)C2=CN=CN=C2c3c[nH]c4ccc(OC5CC5)cc34)CCN6CCN(CC6)CC7CCN(C7)C8=CC=C9C(=O)N(C(=O)C8)C(=O)N9CC1(C)OC(c2ccc3c(c2)c[nH]3)c4ncnc4N5CCN(CC5CCN6CCN(CC6)C(=O)N7CCCC7C(=O)O)c8ccccc8

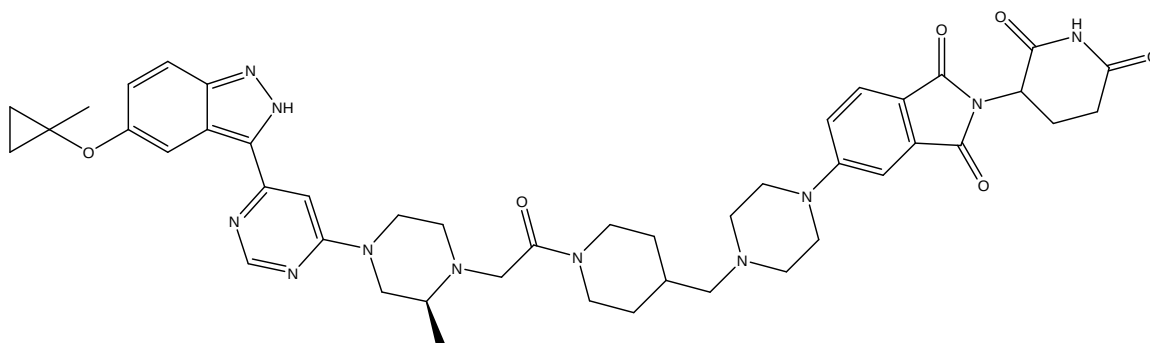
(56),



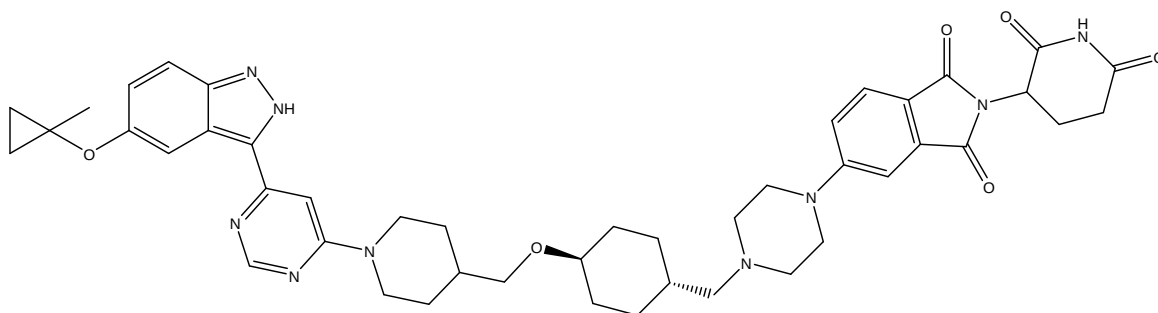
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(58),



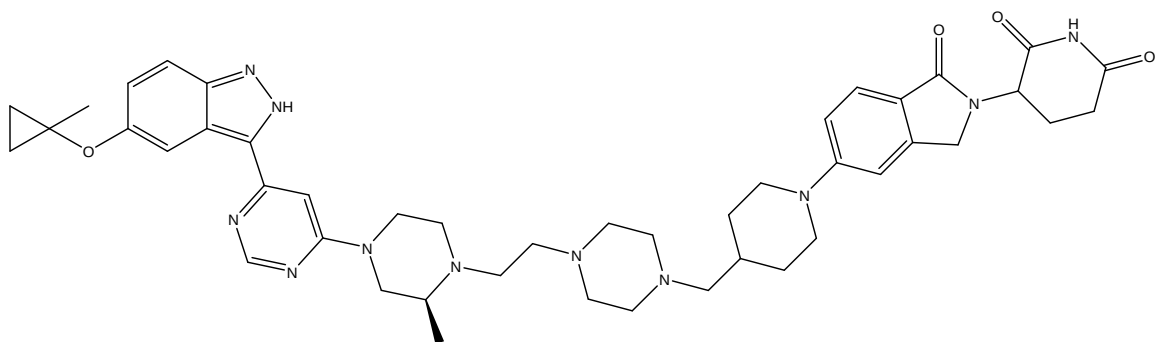
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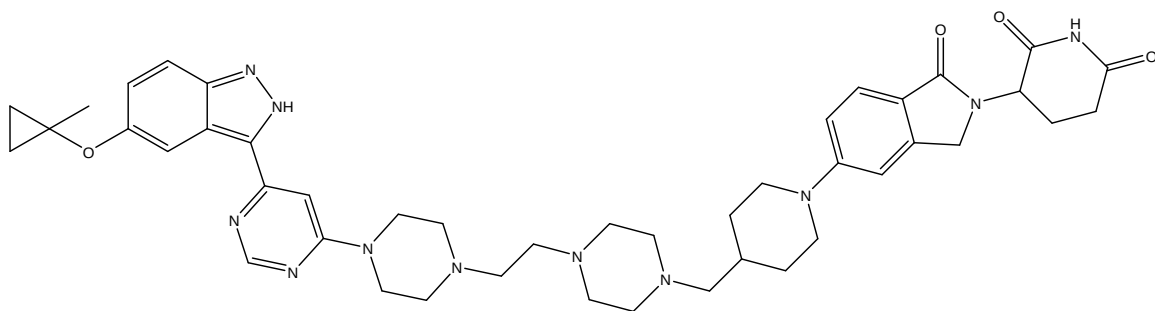
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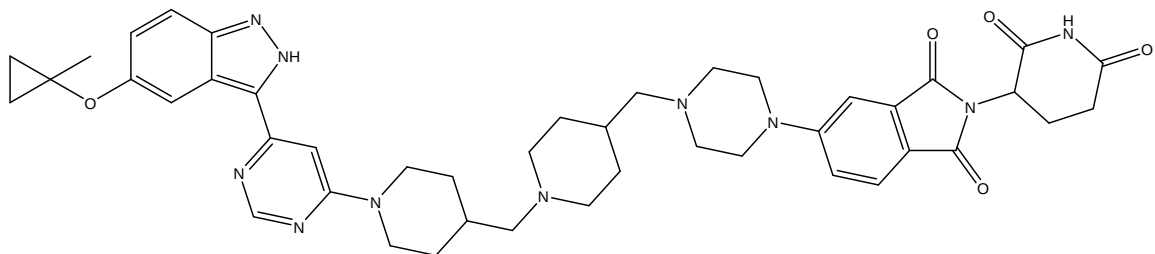
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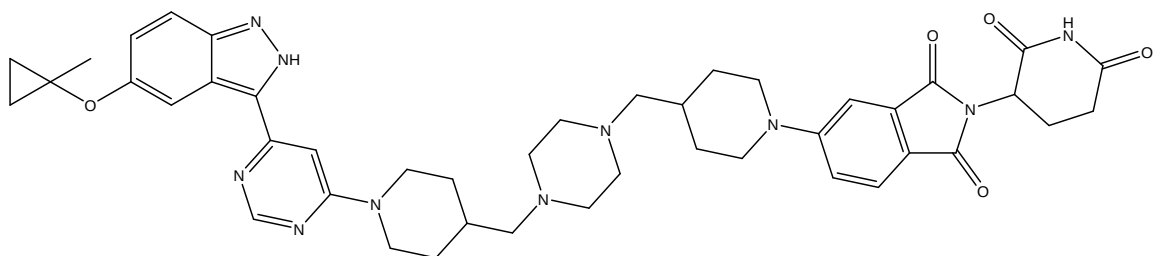
(65),



(66),



(67),



(68),

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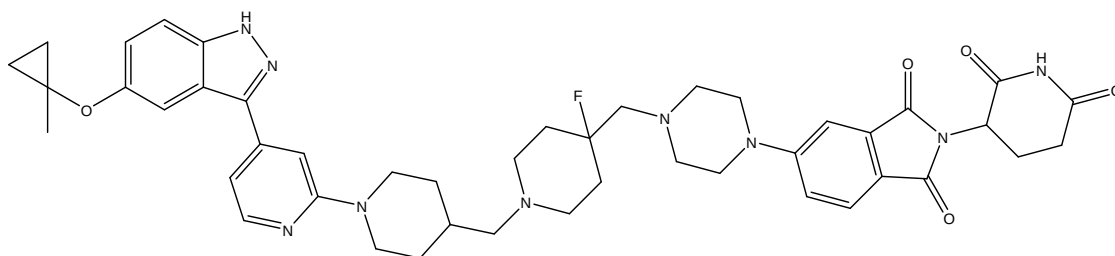
(72),

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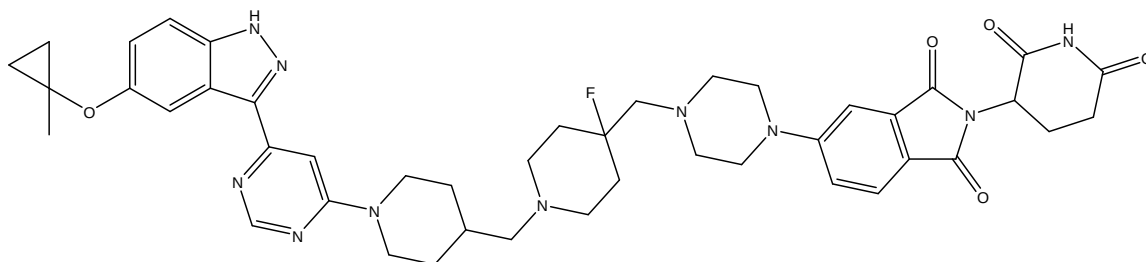
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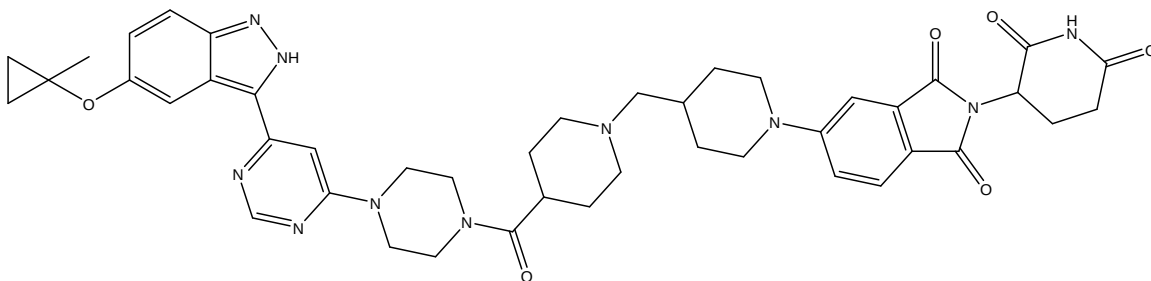
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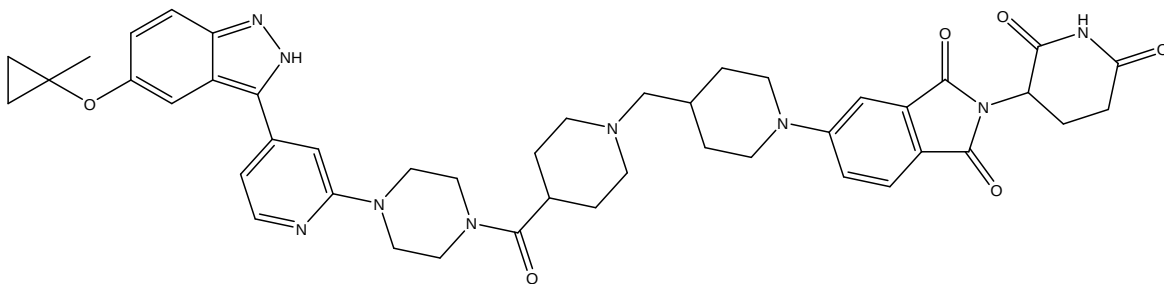
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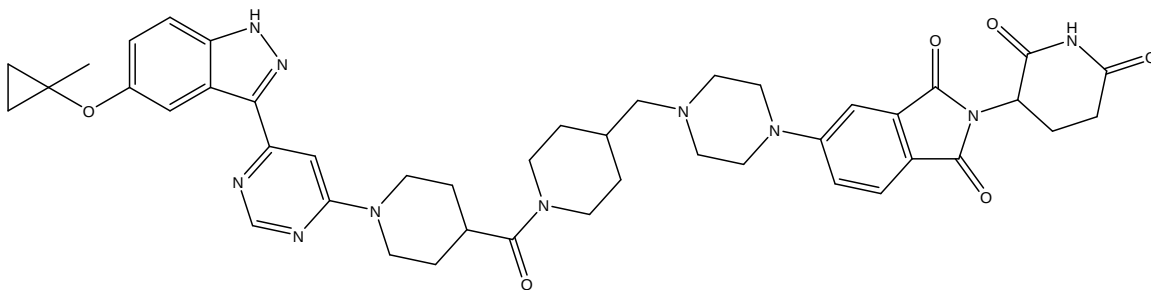
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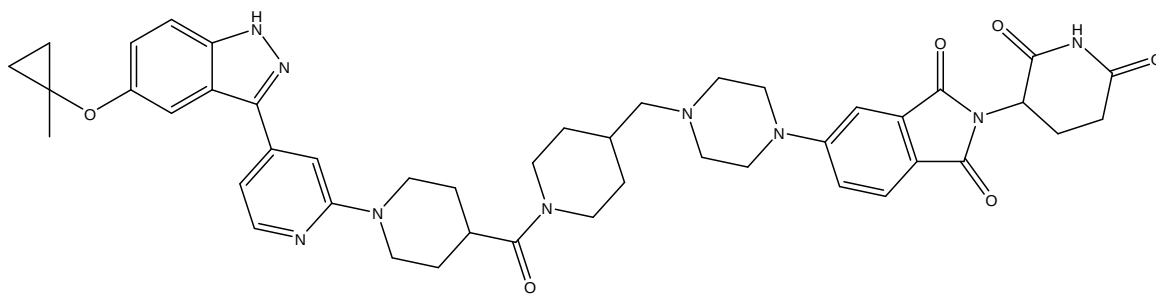
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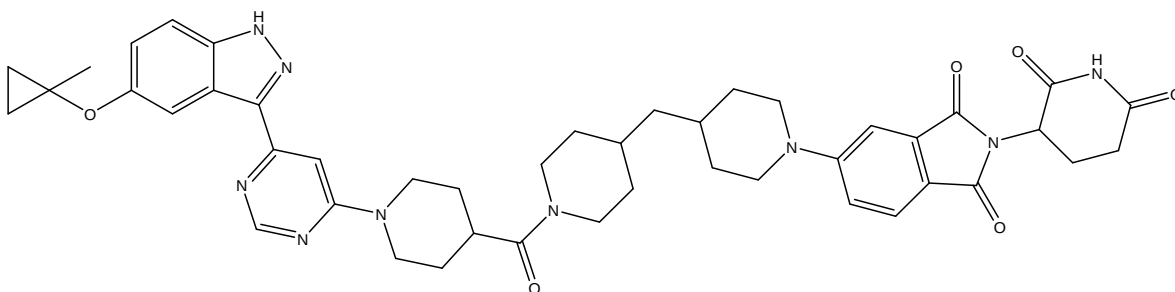
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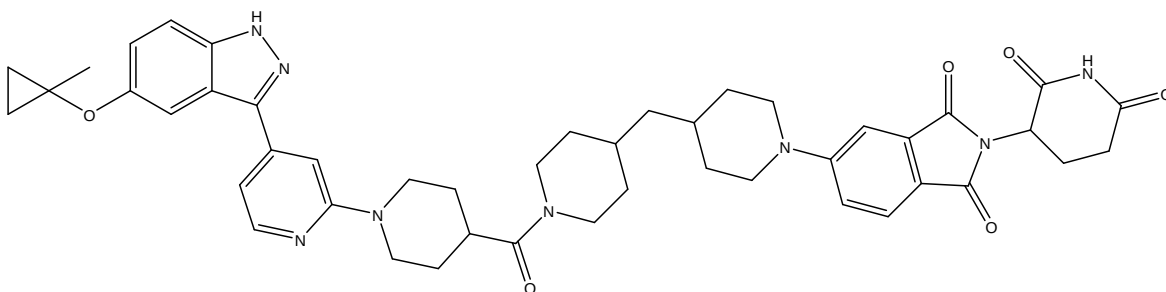
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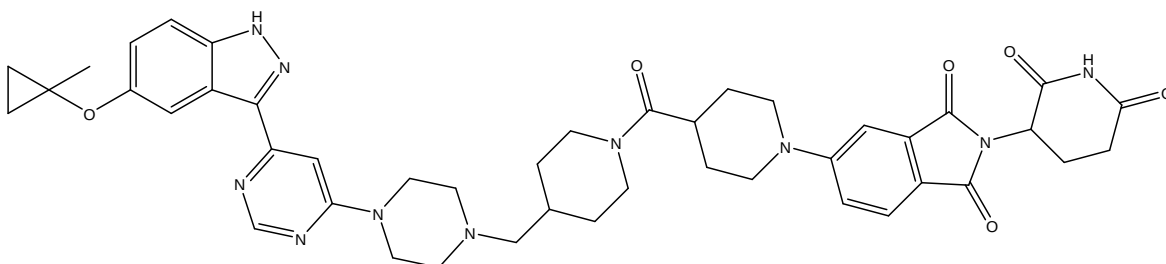
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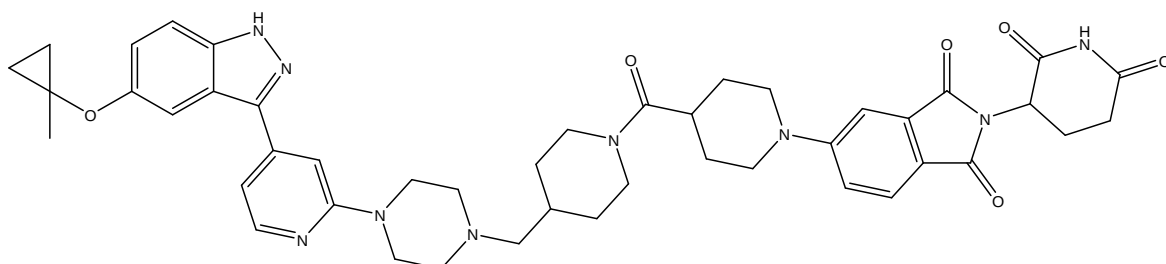
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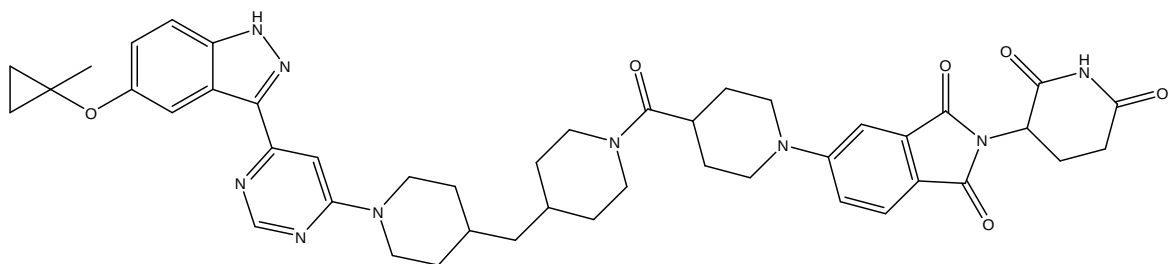
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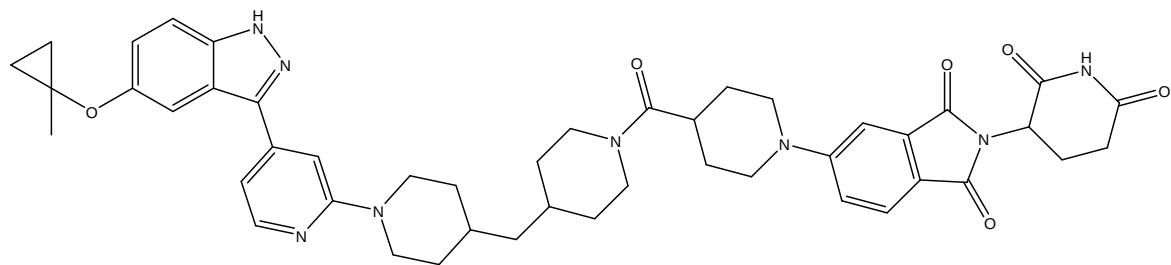
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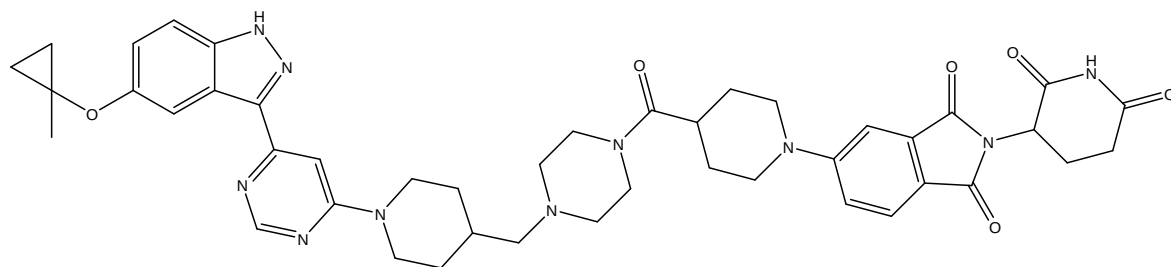
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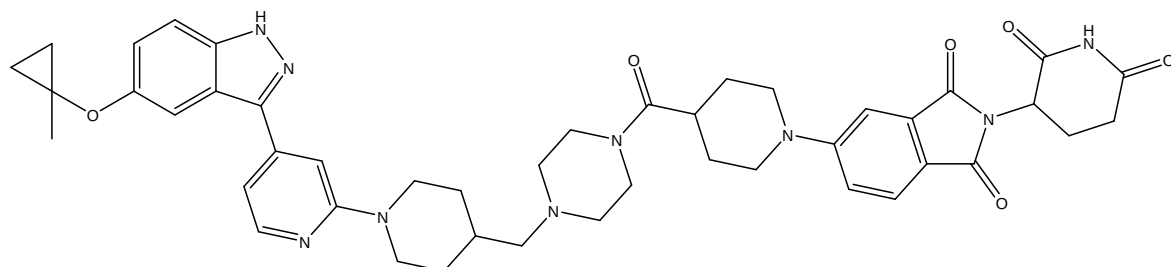
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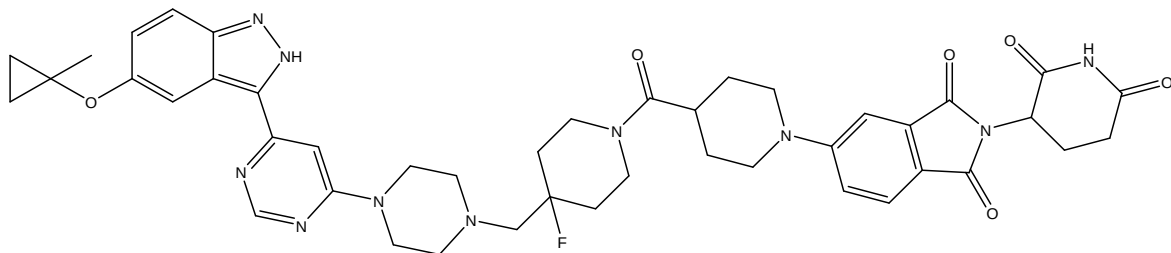
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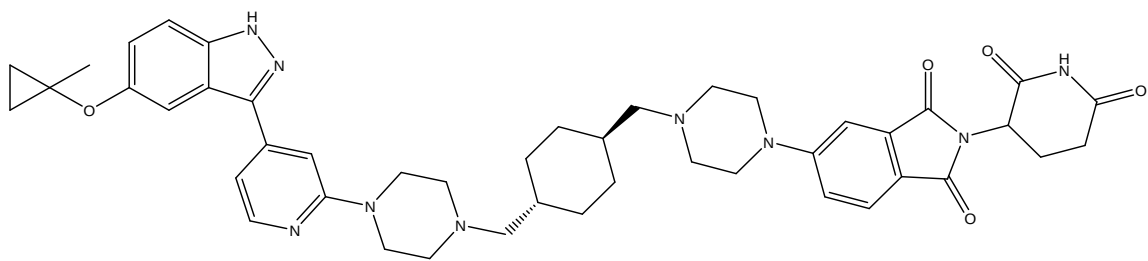
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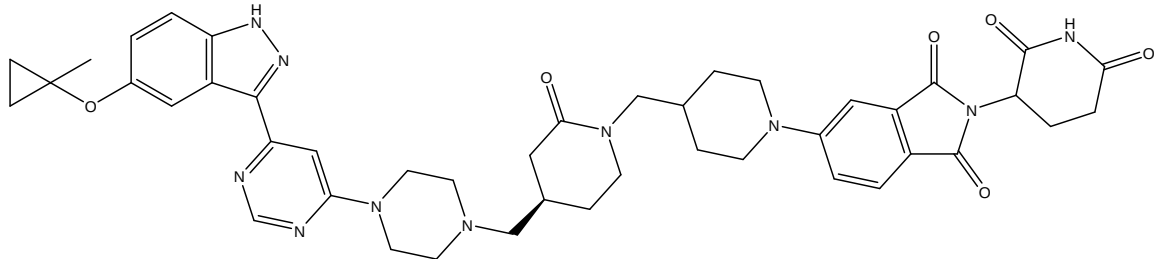
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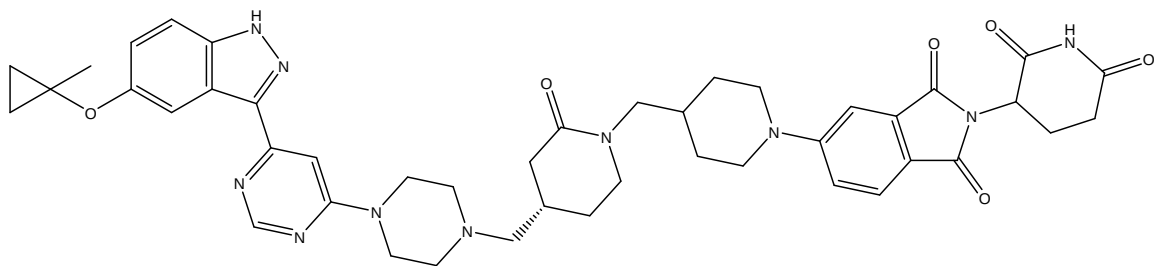
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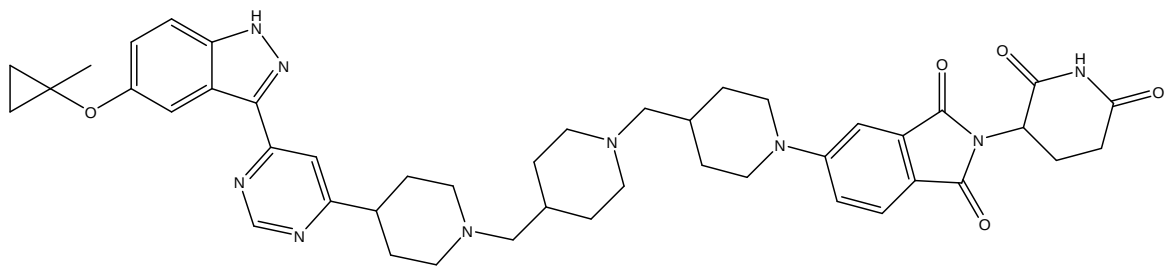
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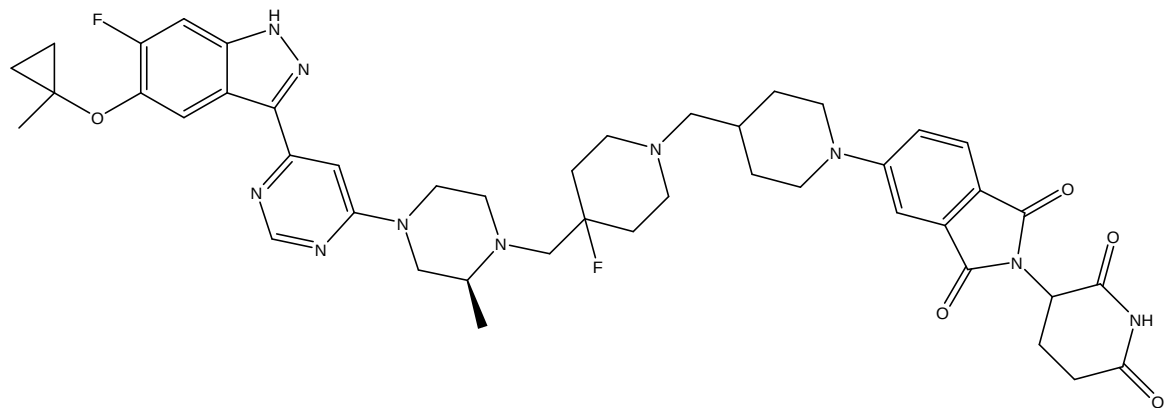
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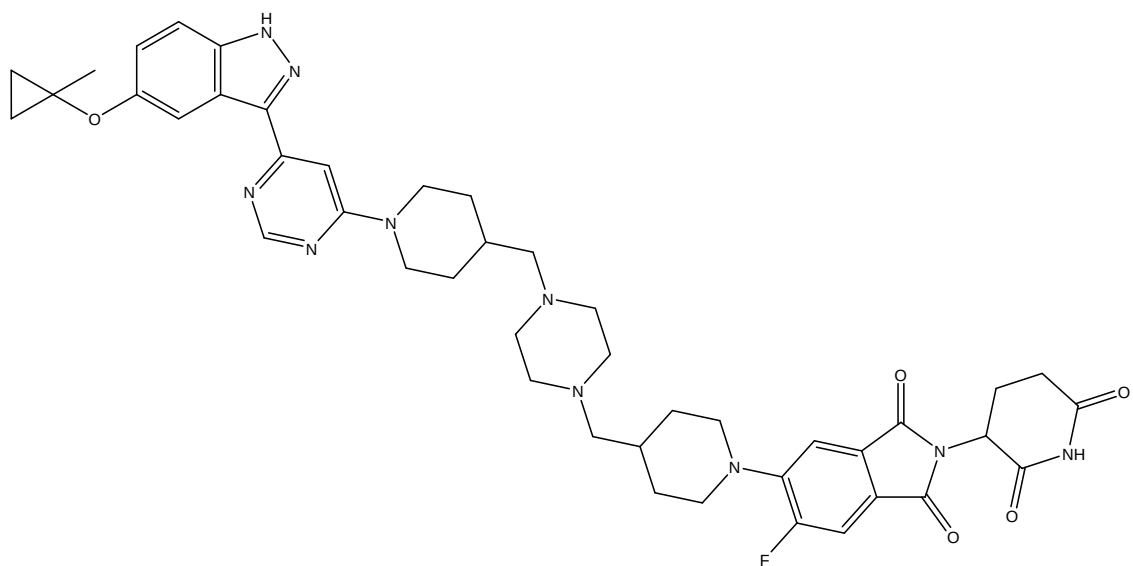
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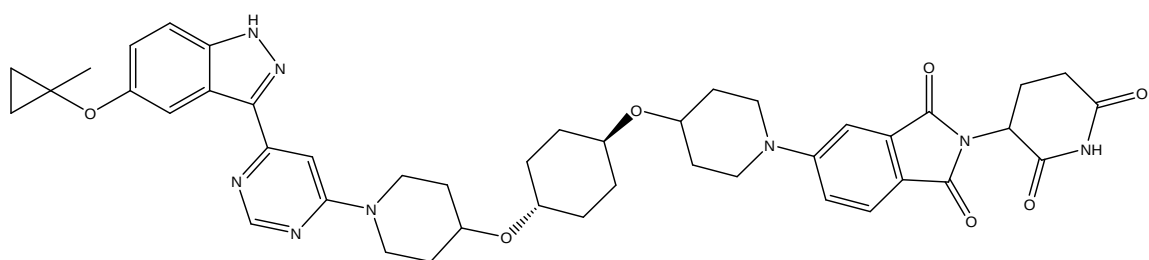
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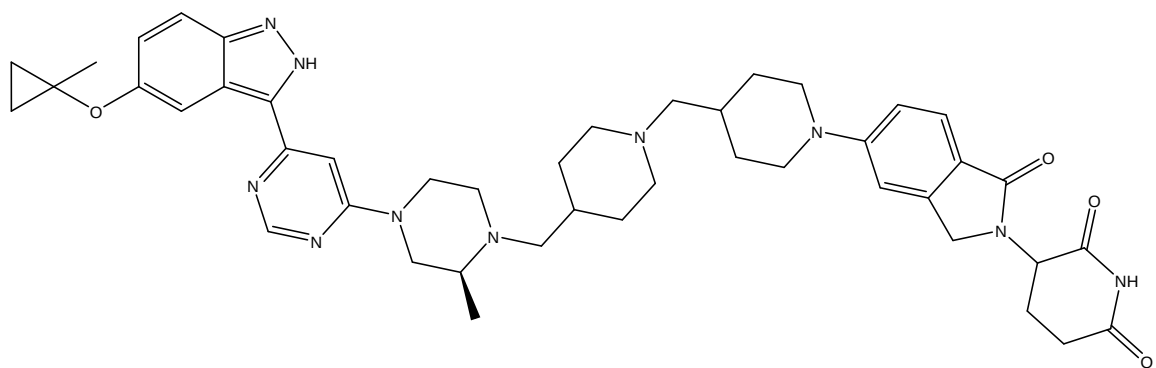
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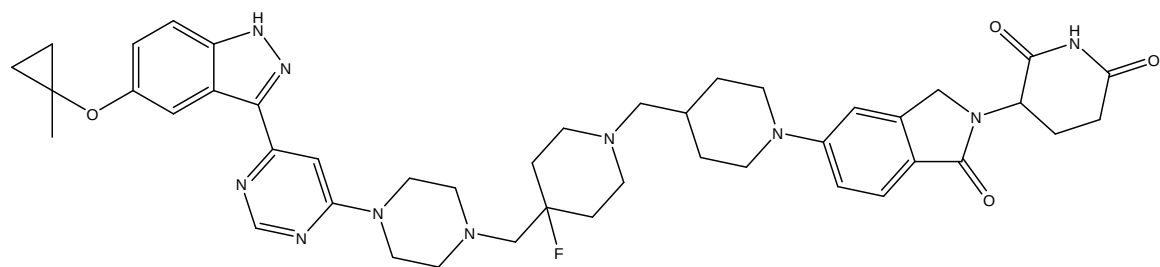
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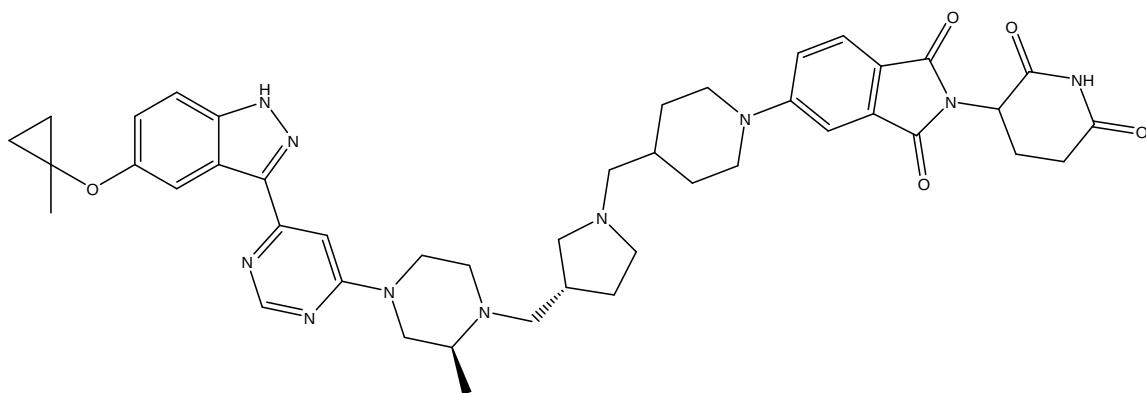
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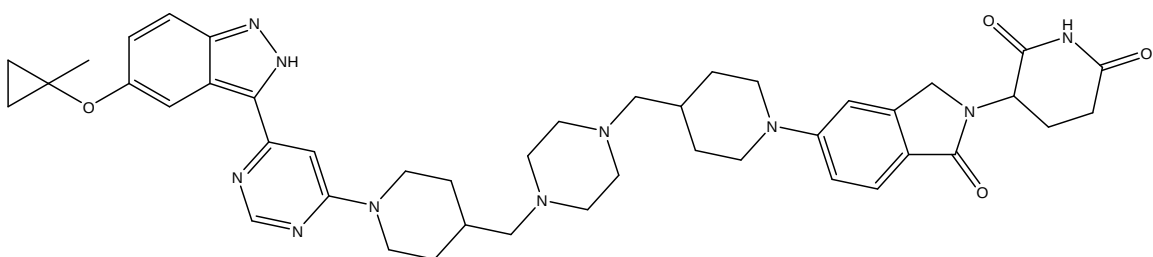
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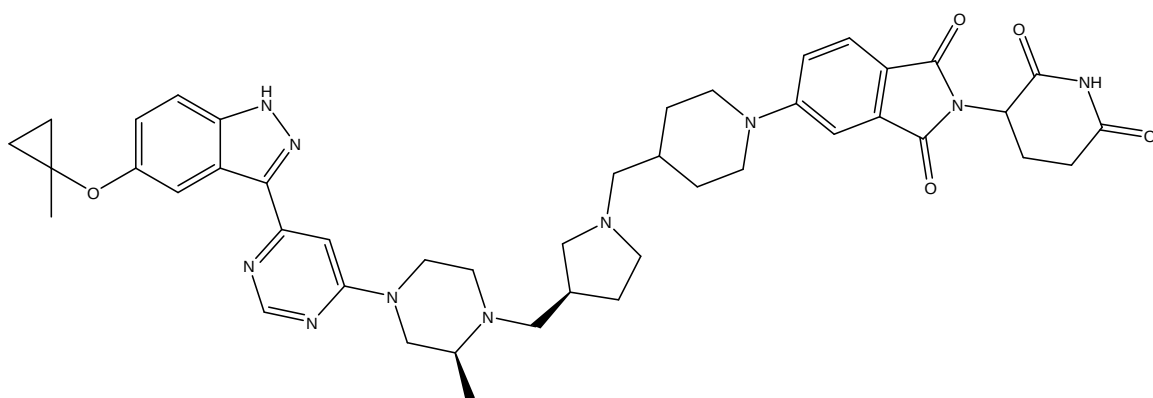
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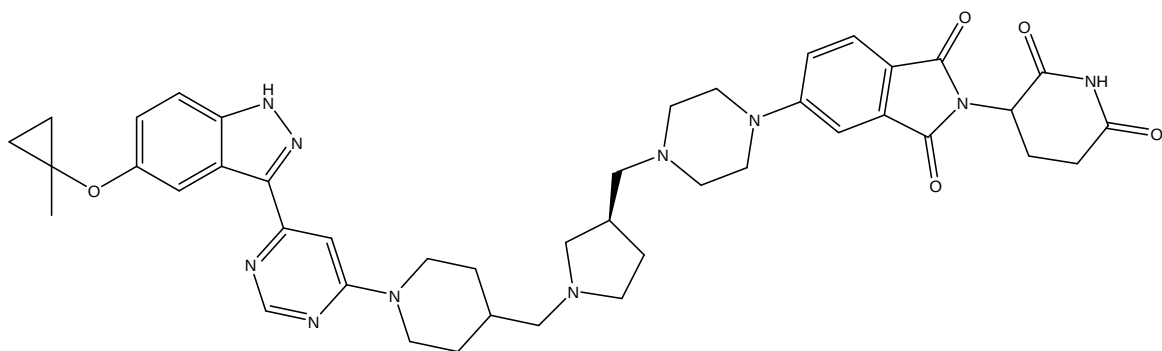
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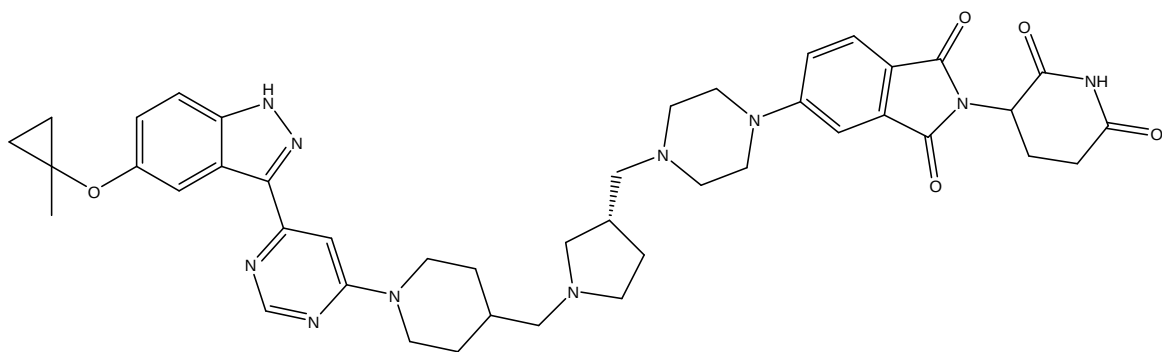
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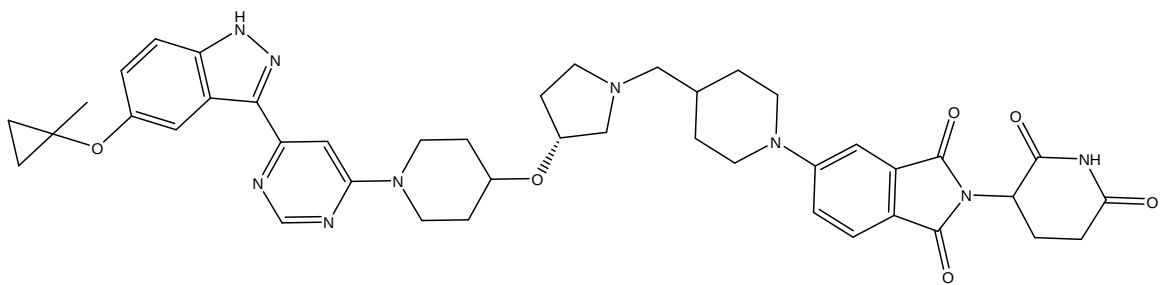
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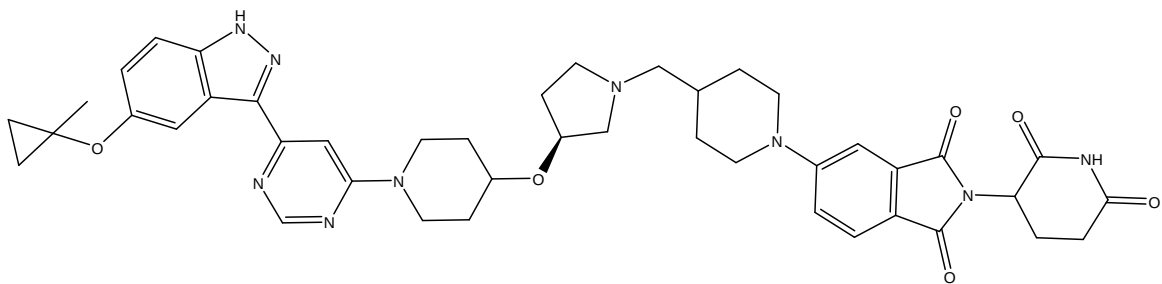
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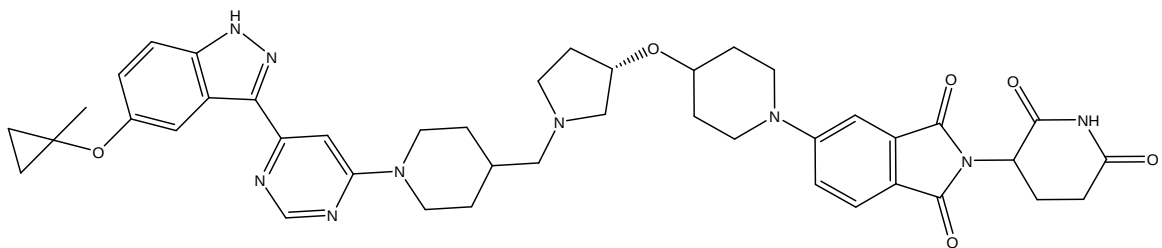
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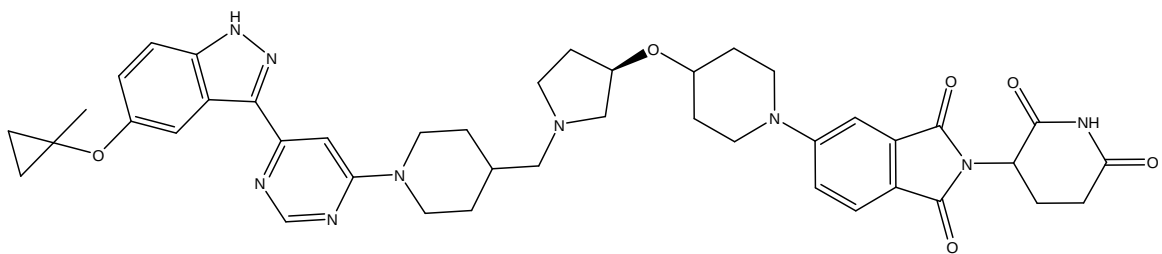
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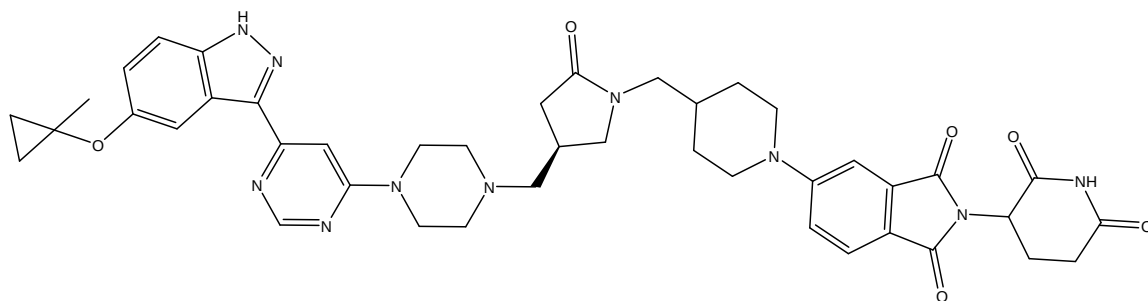
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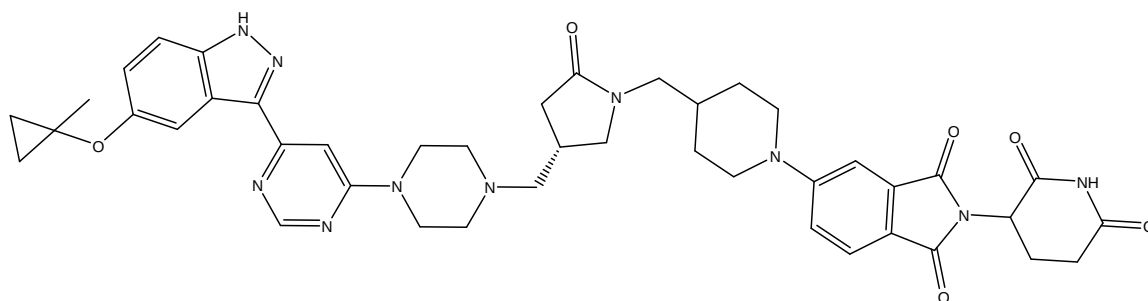
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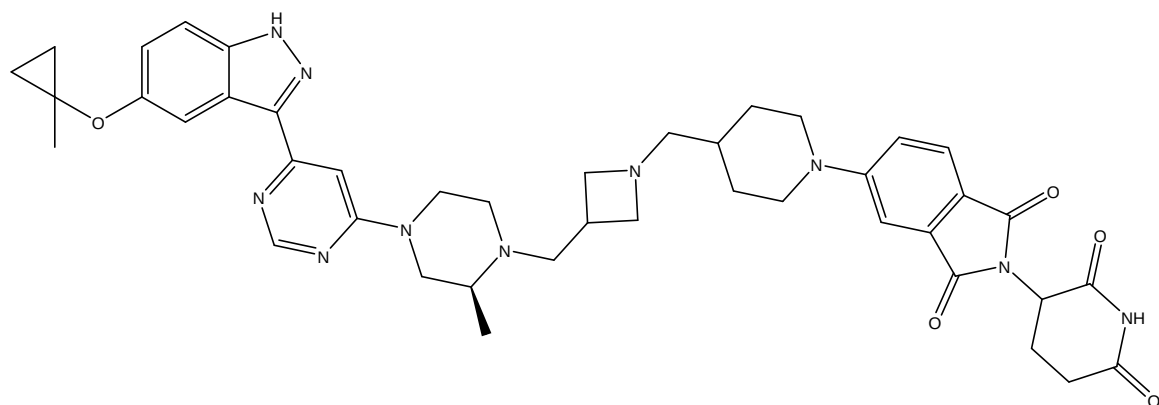
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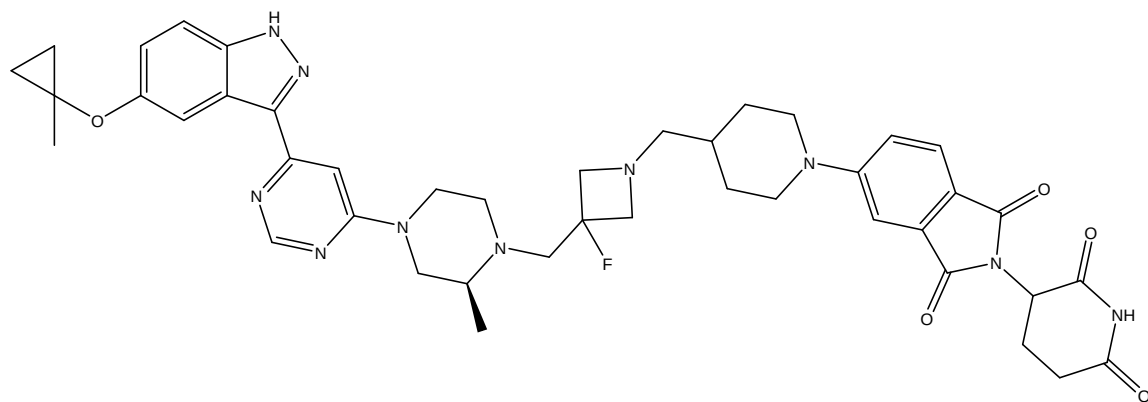
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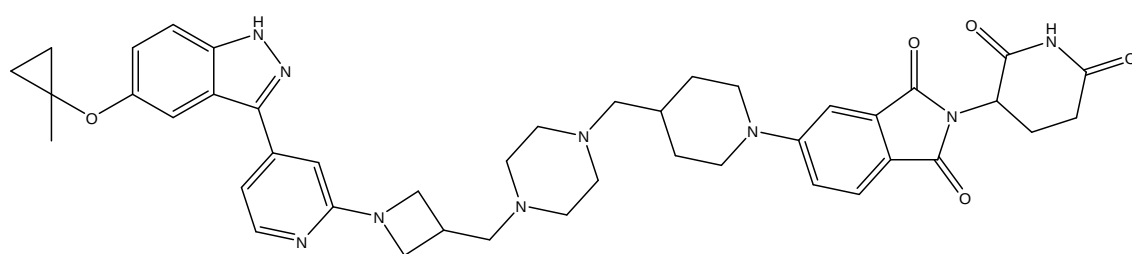
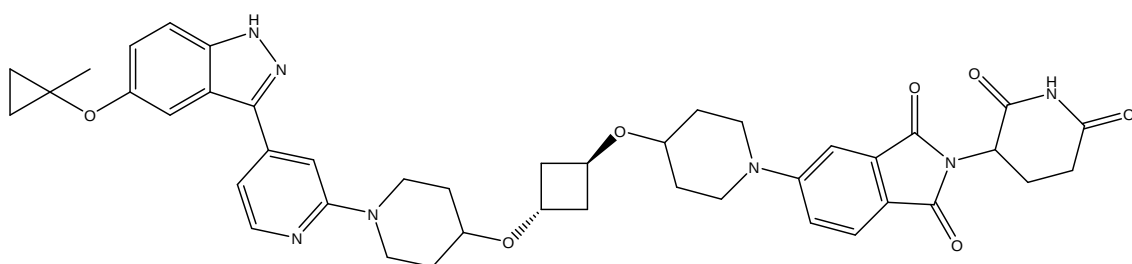
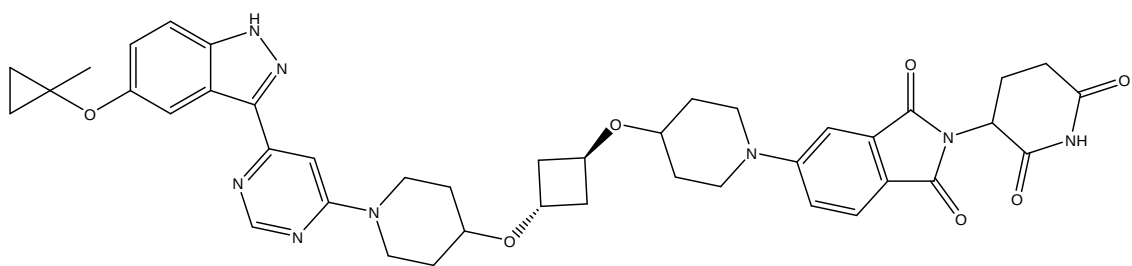
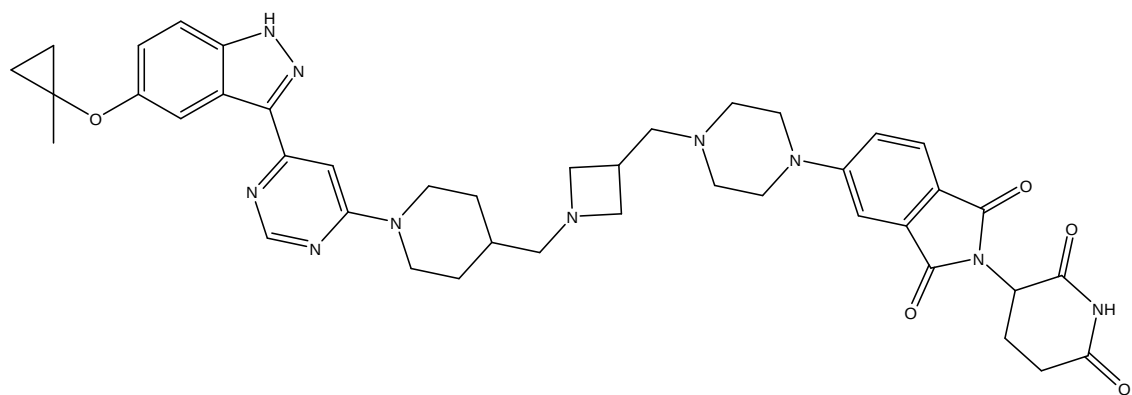
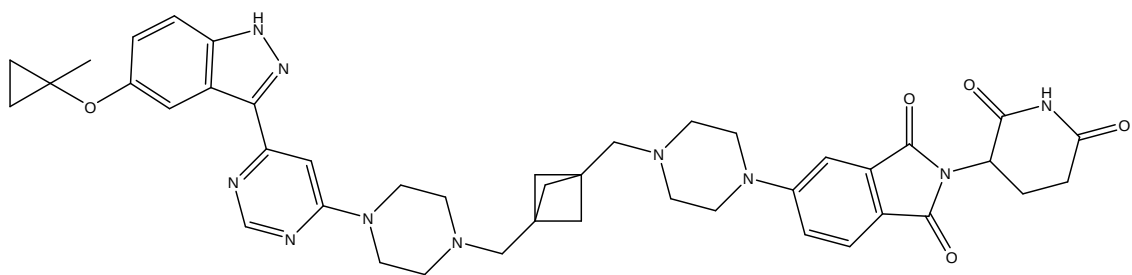
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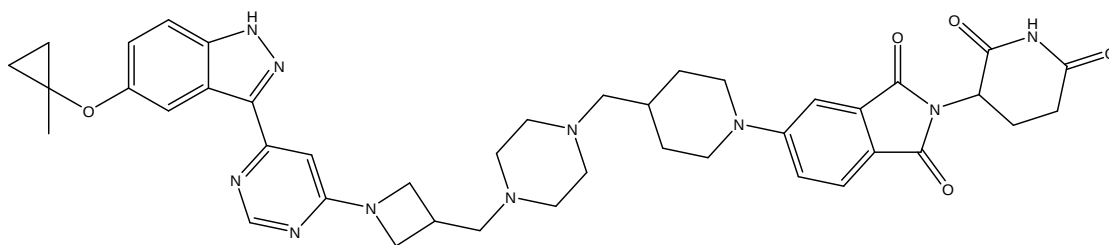
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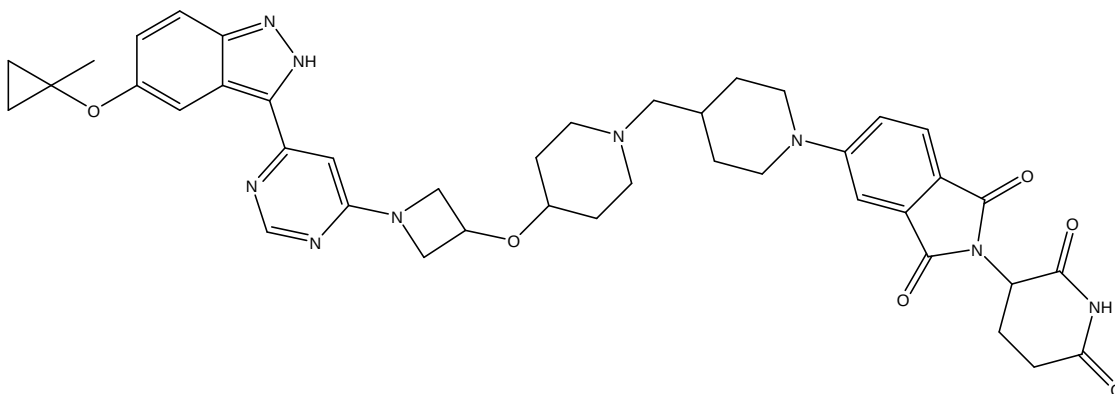
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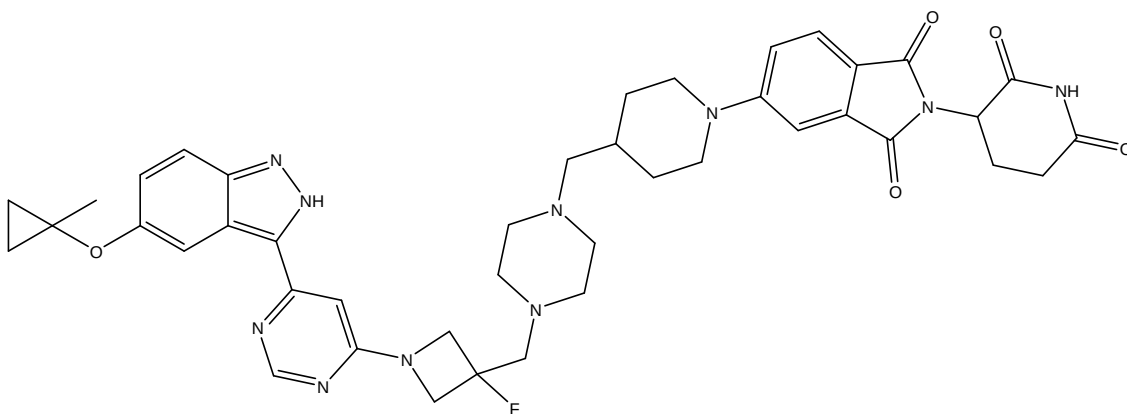
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(129),

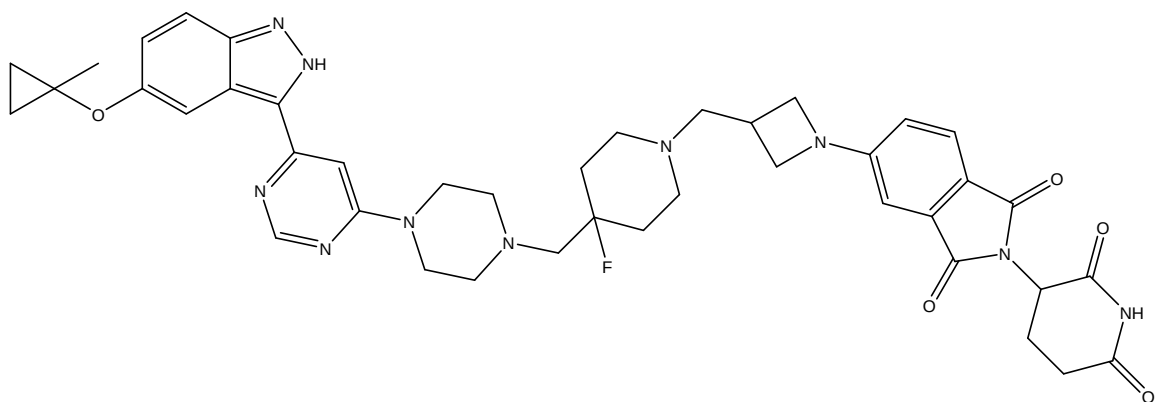


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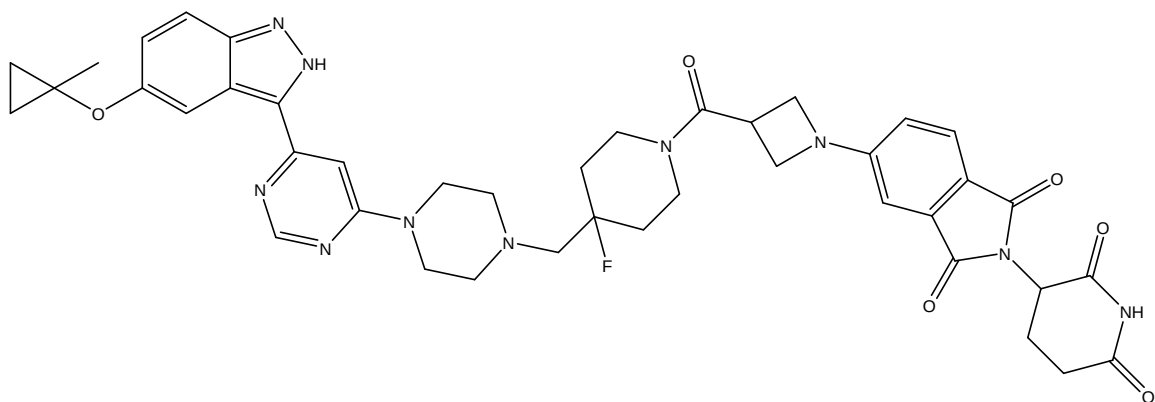


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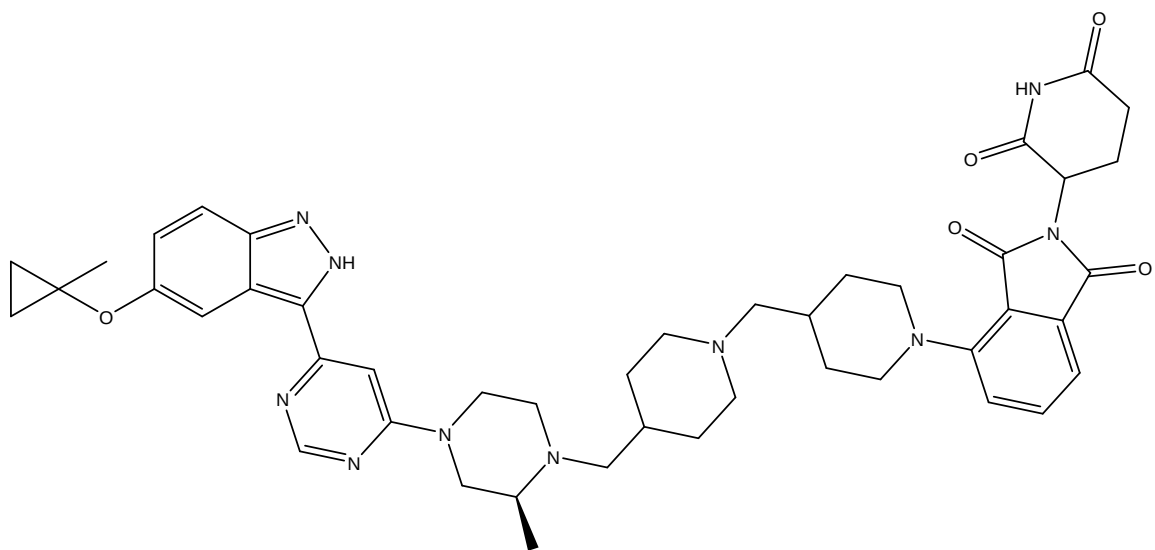
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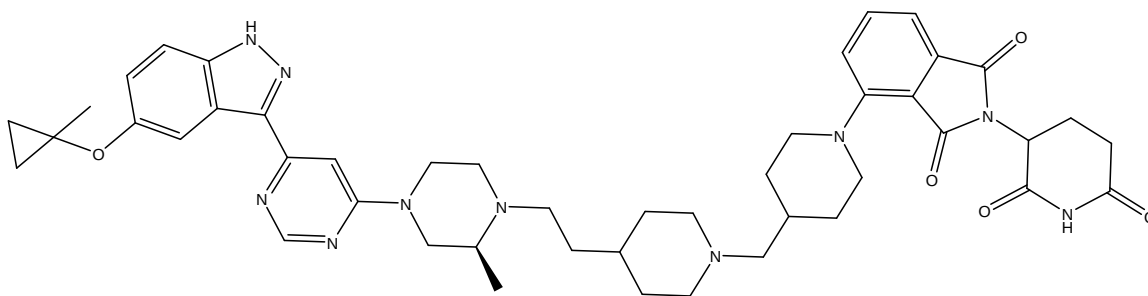
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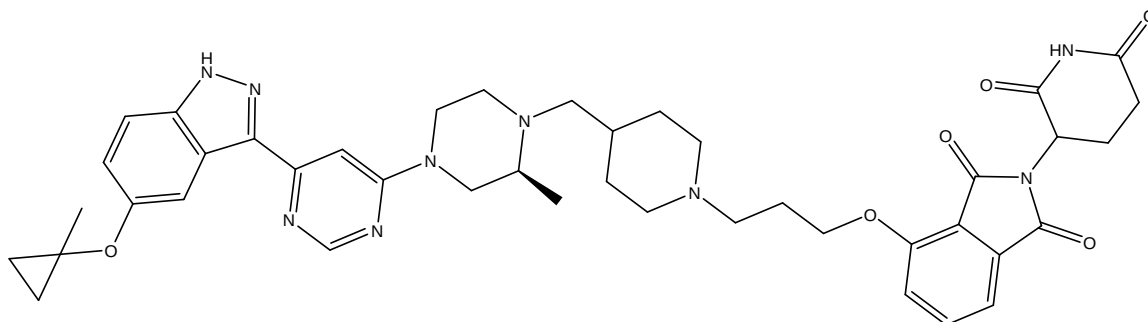
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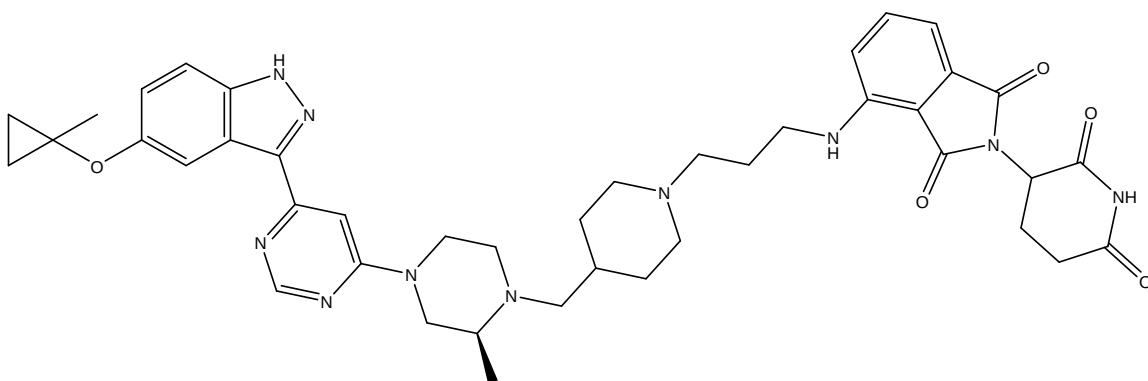
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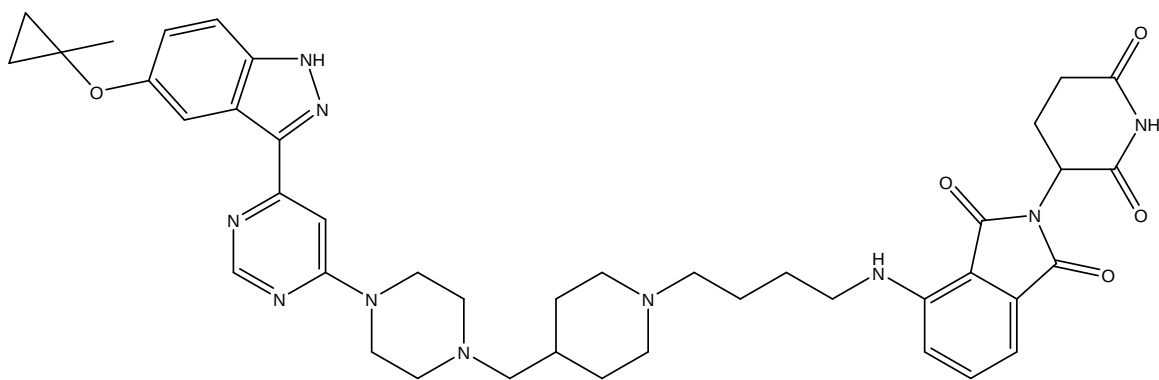
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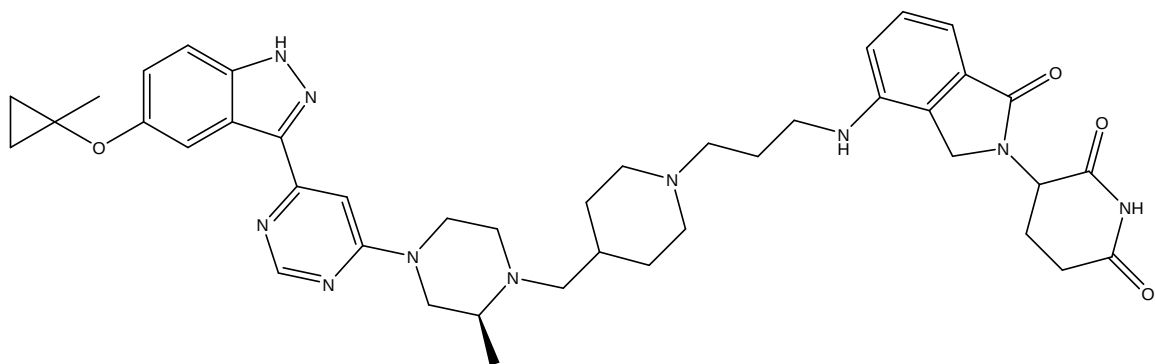
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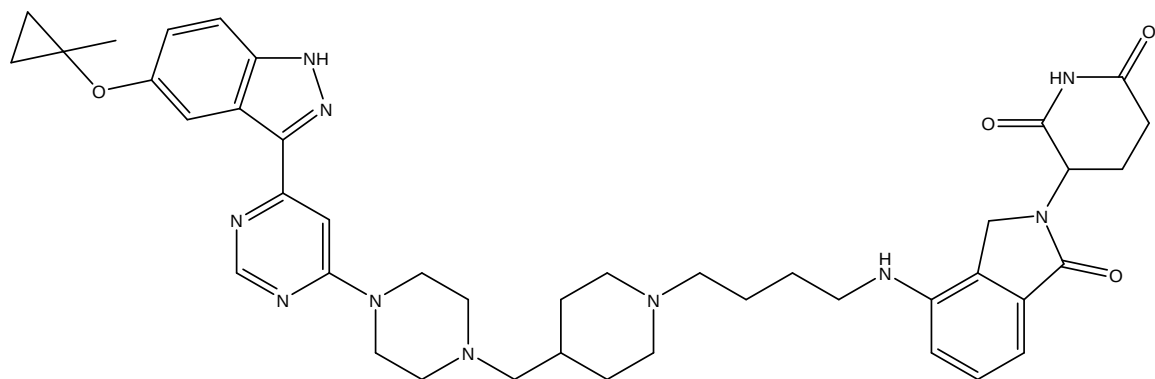
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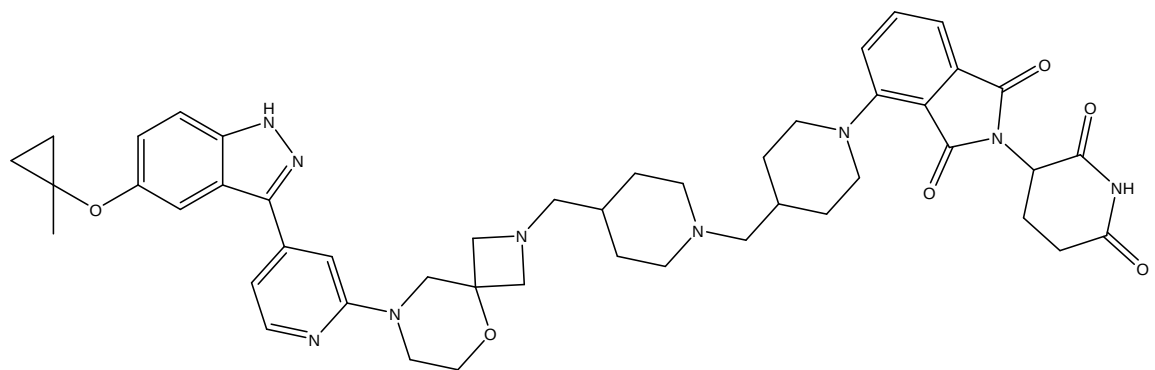
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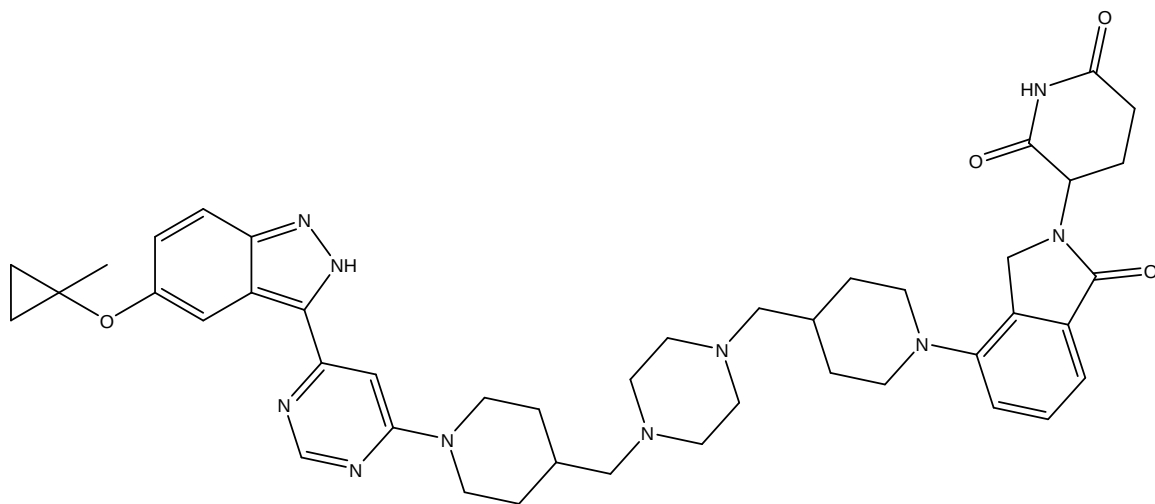
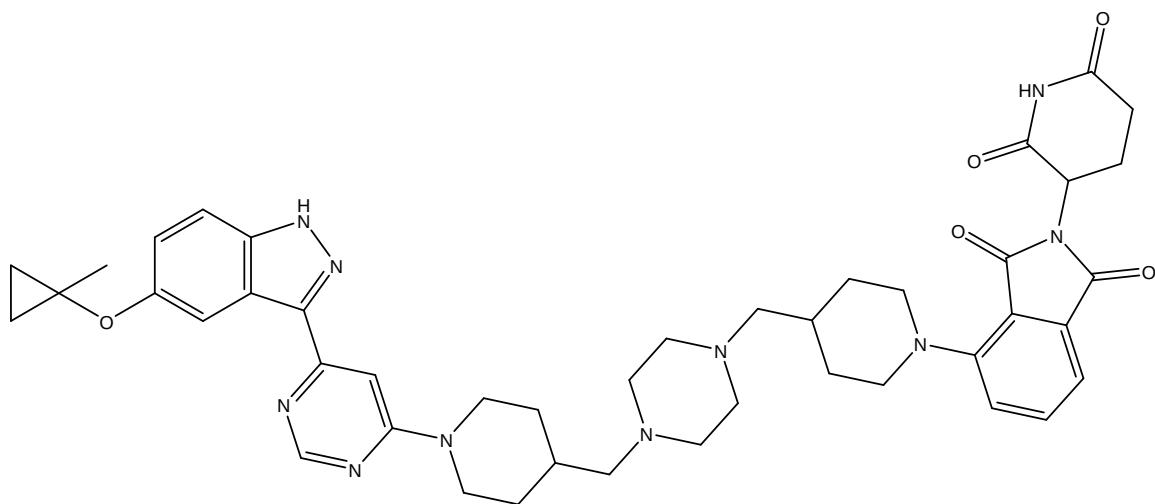
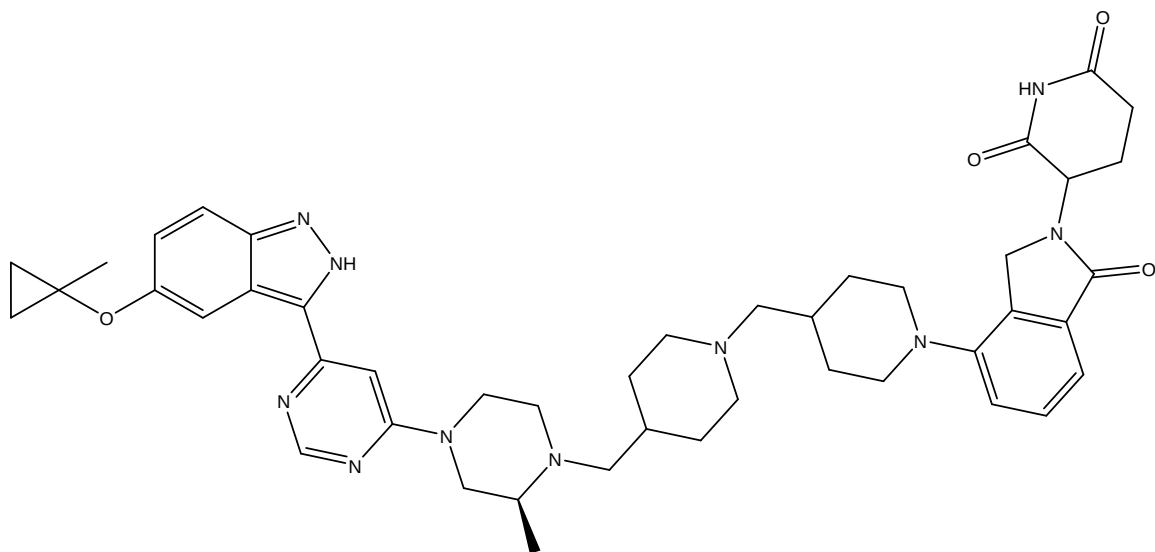
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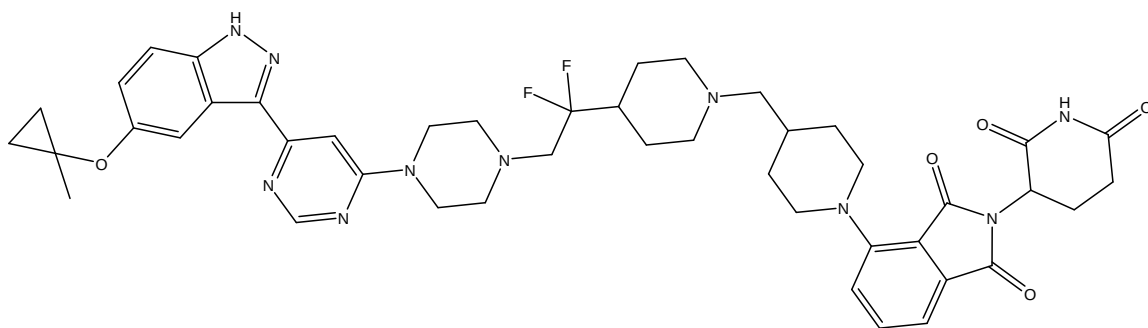
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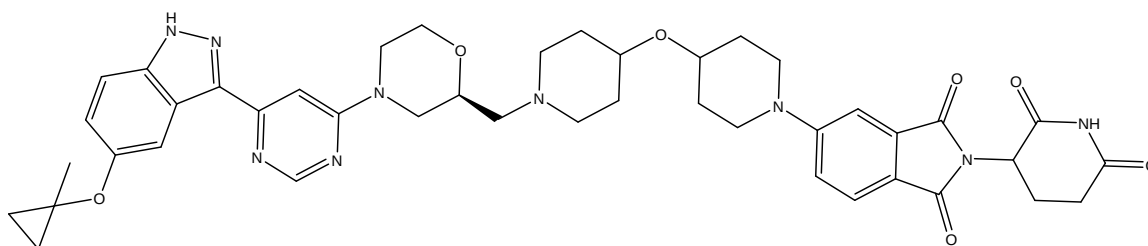
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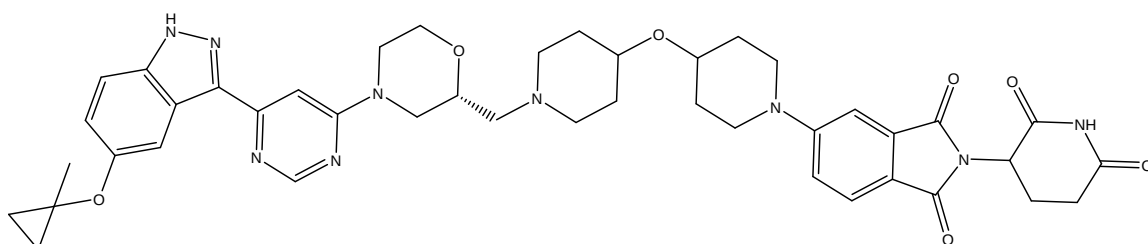
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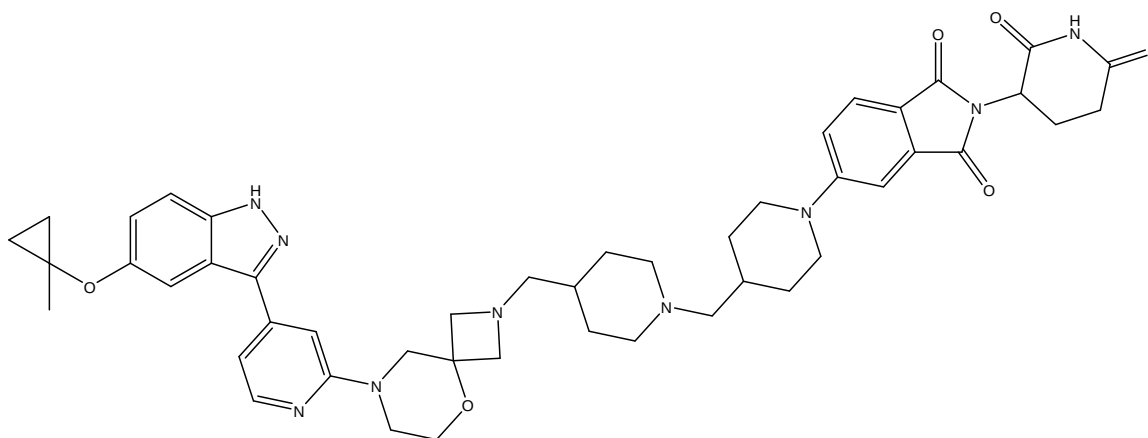
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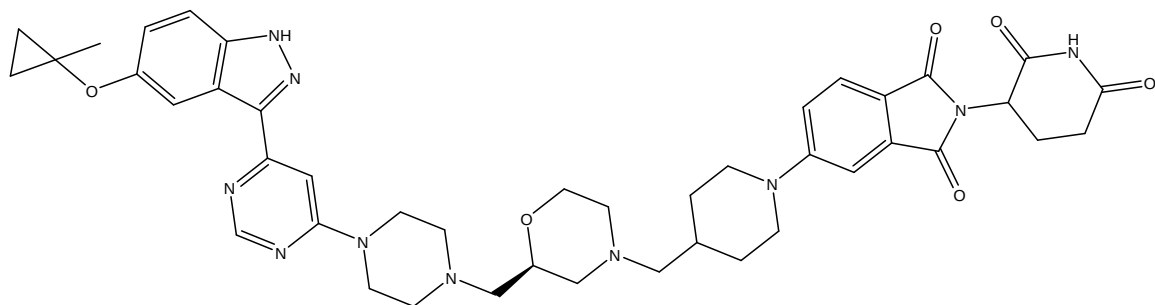
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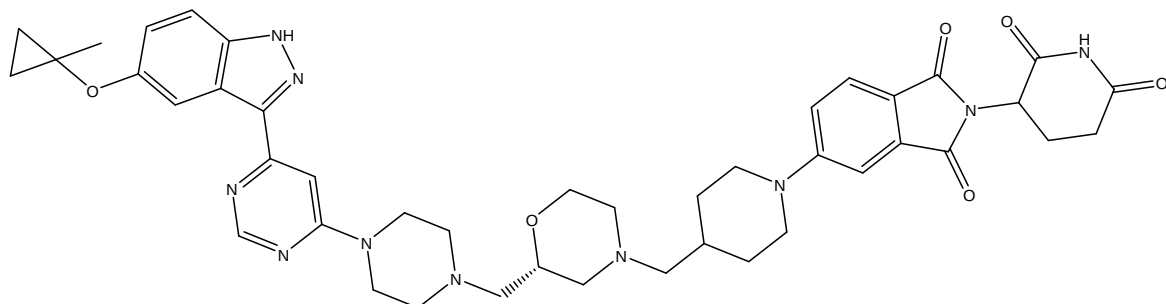
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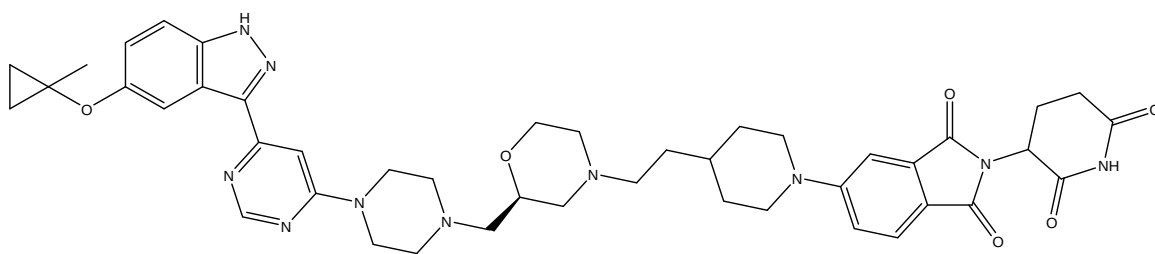
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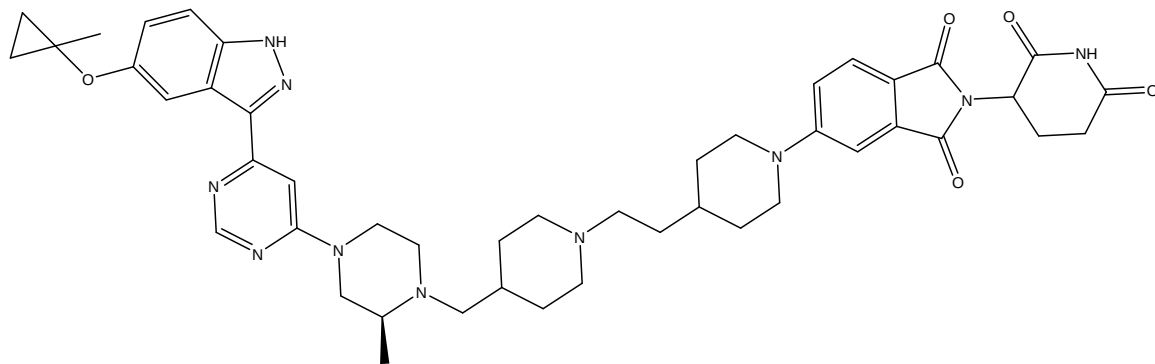
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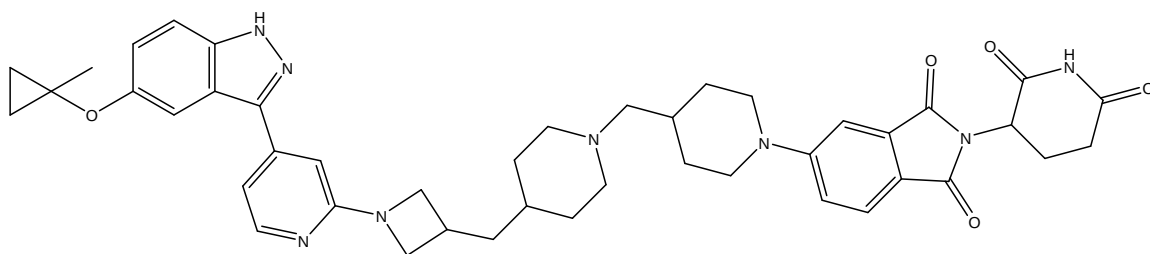
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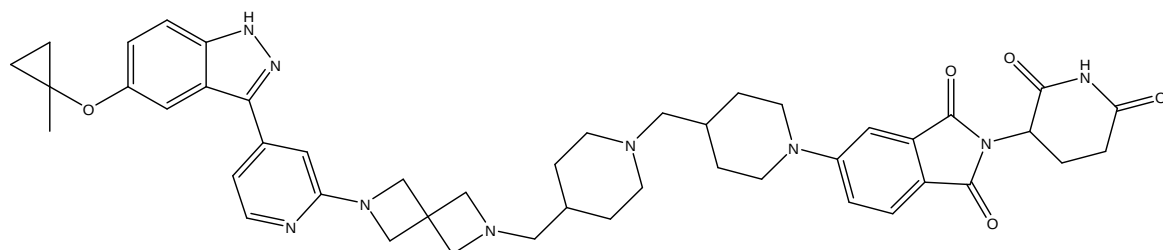
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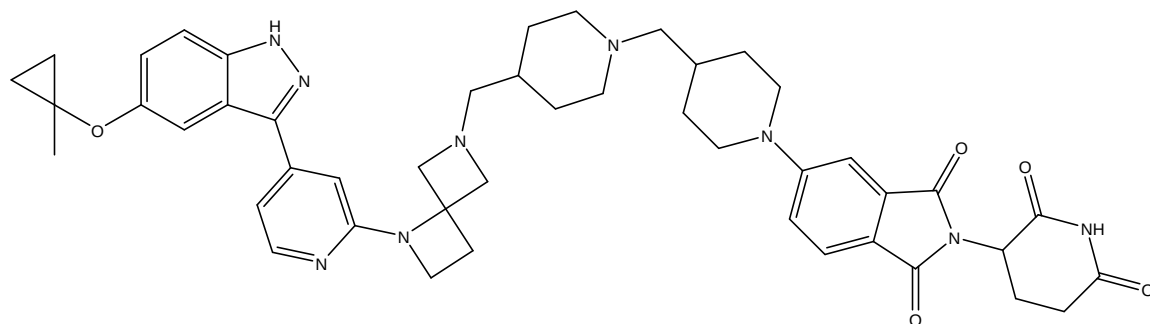
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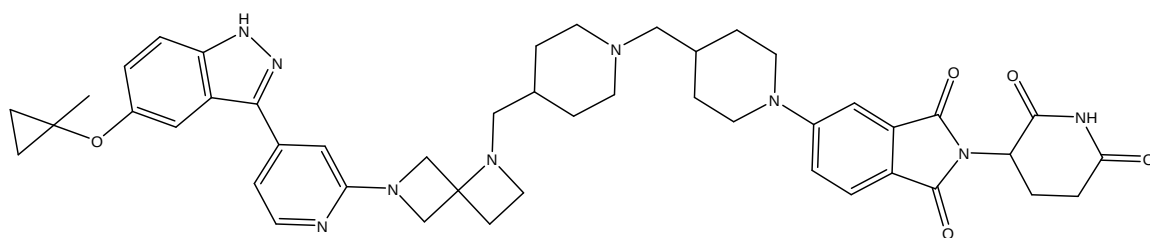
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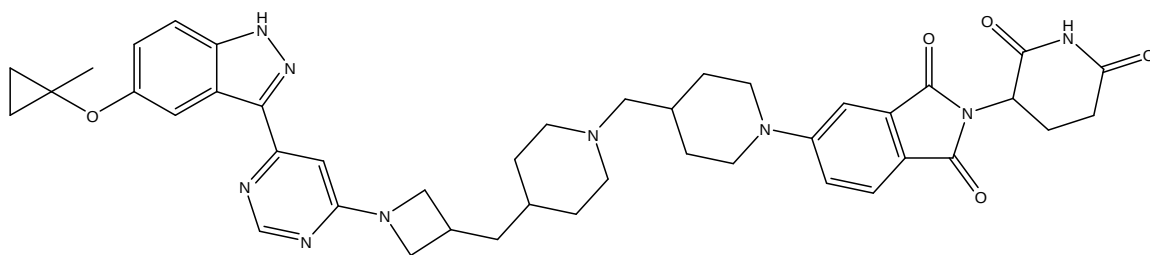
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(162),

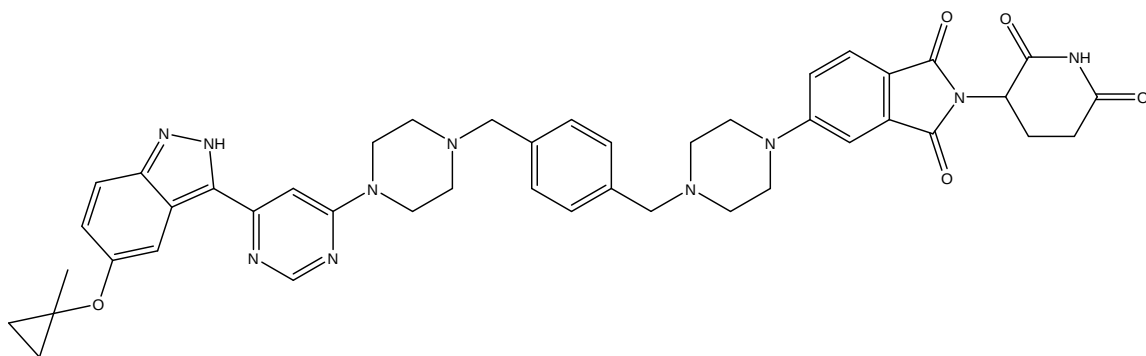


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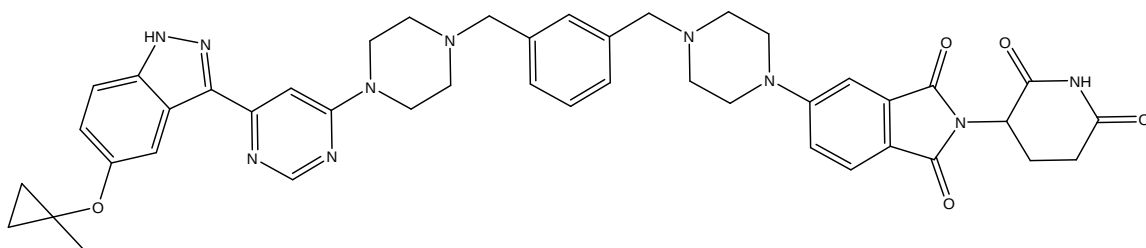


(164),

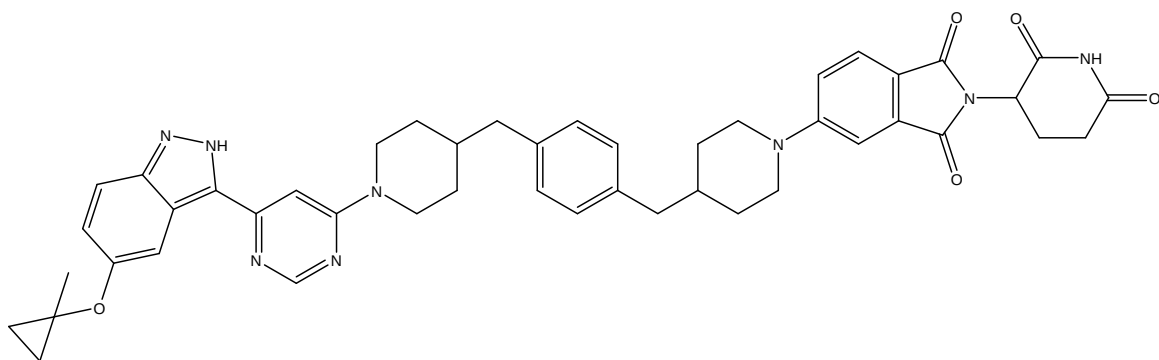
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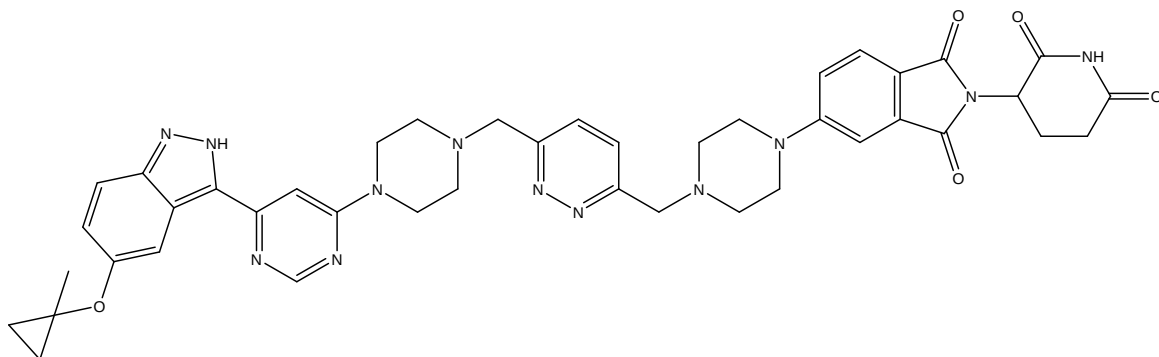
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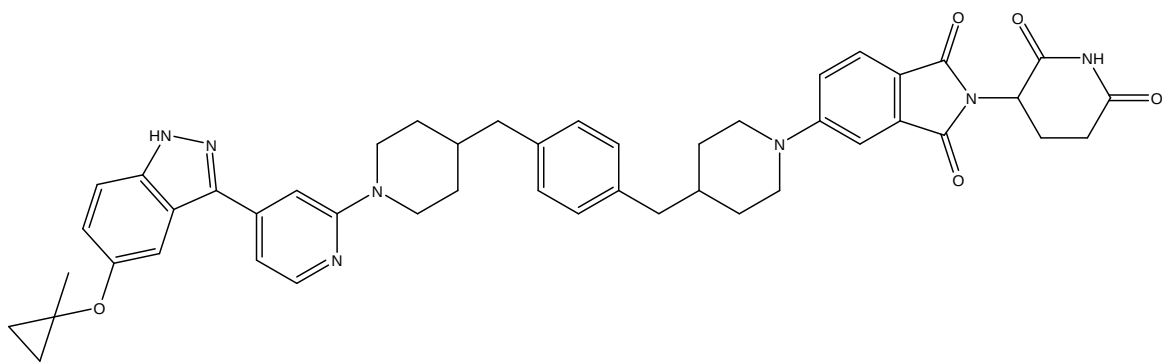
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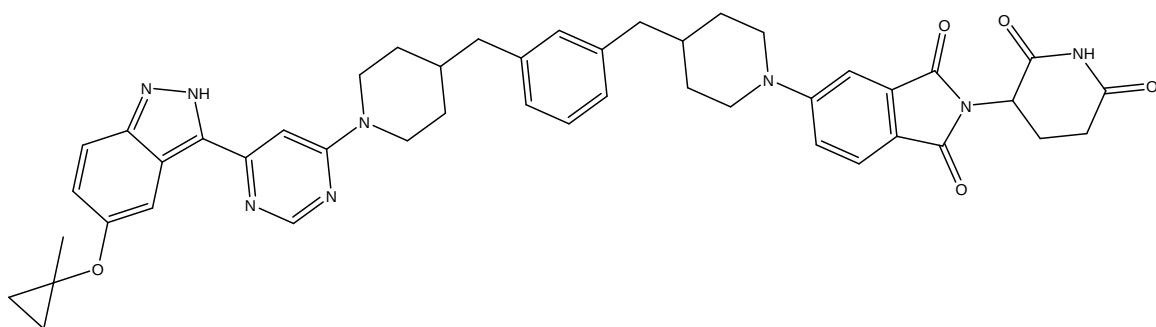
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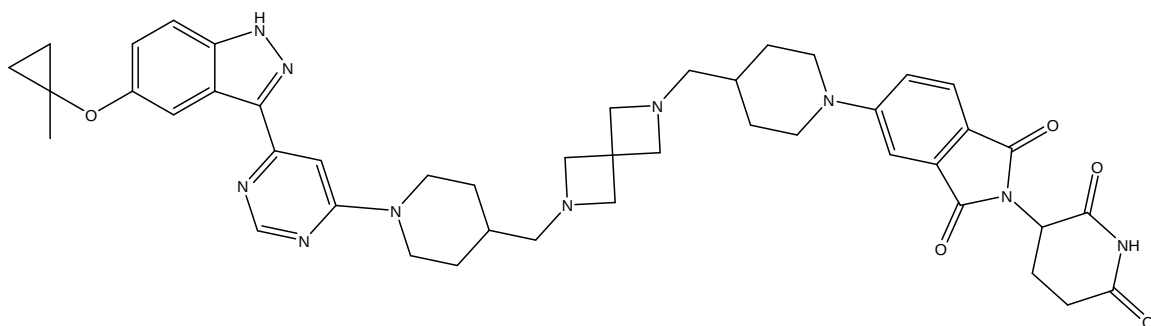
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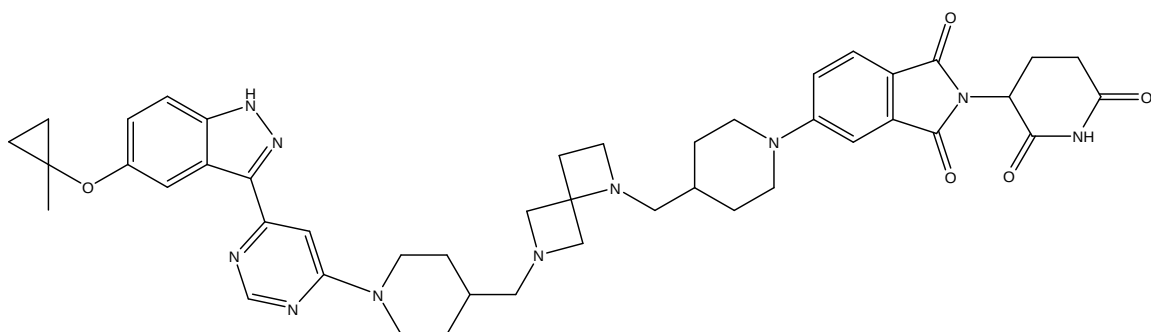
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(174),



(175),



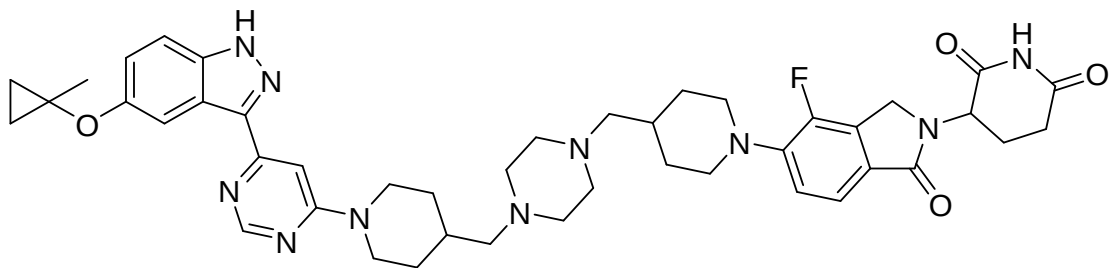
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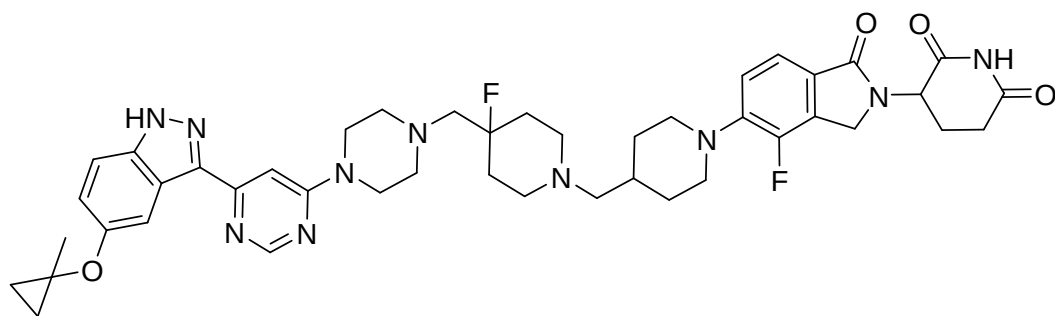
(179),

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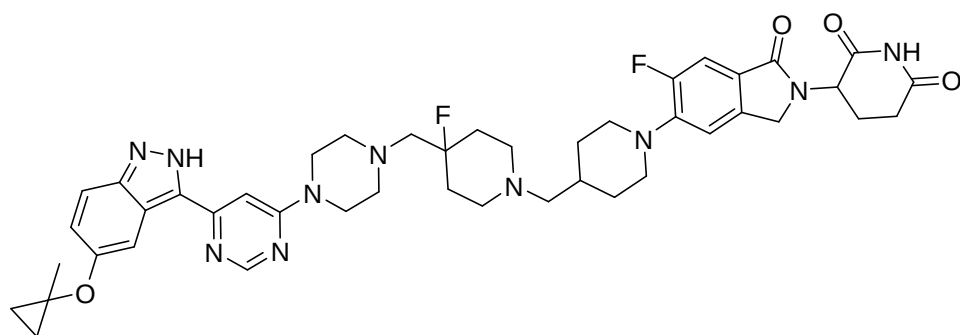
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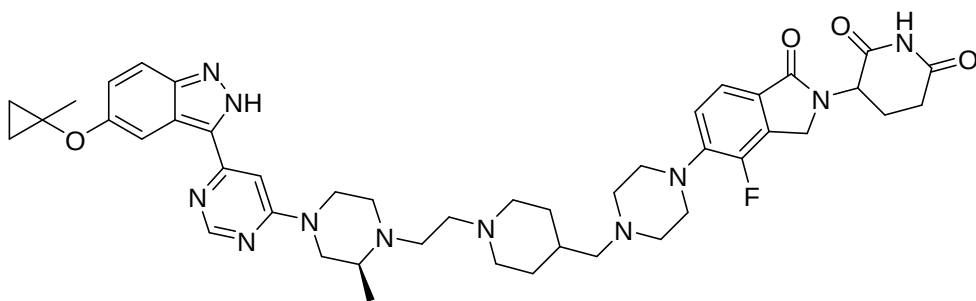
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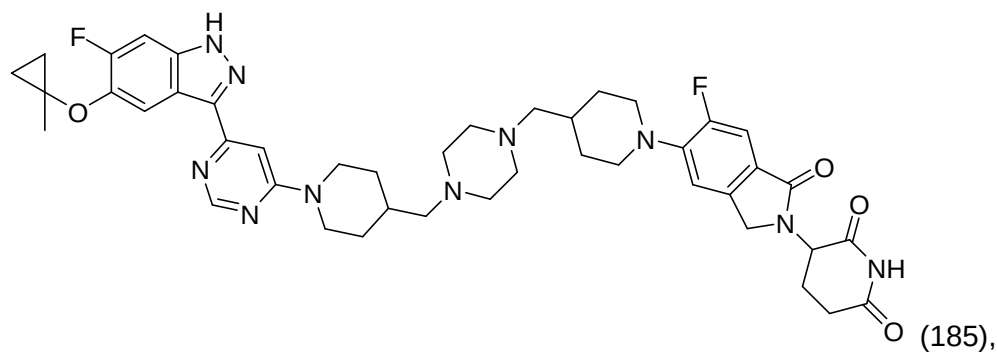
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(183),



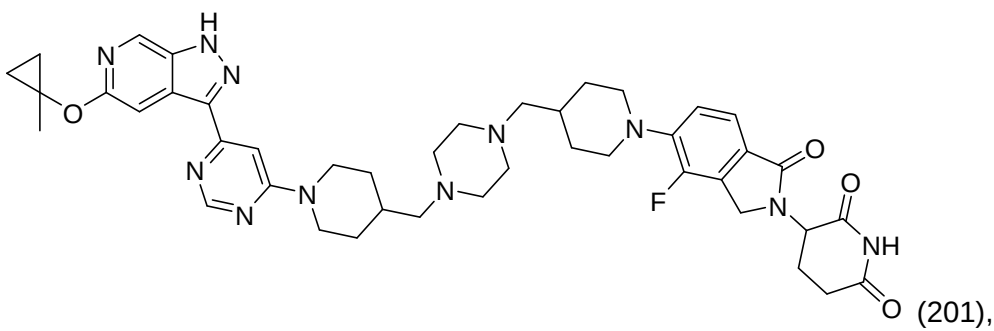
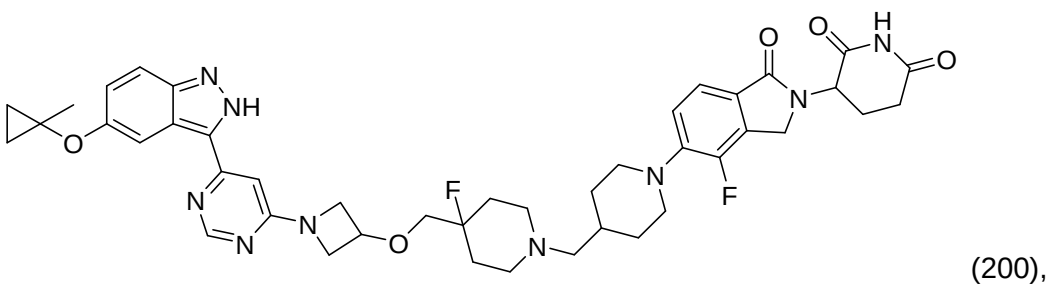
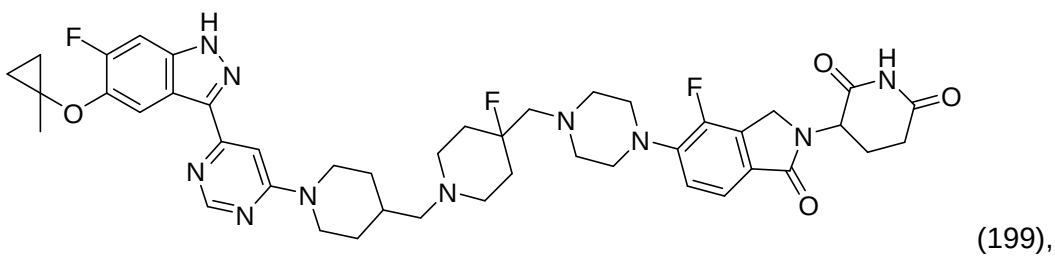
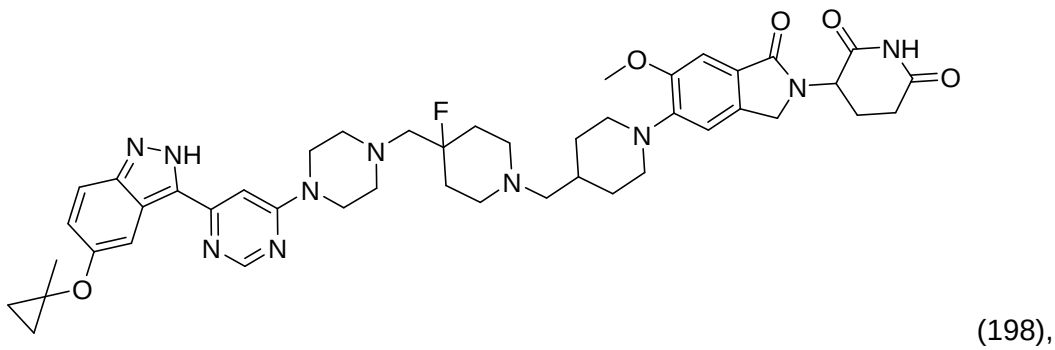
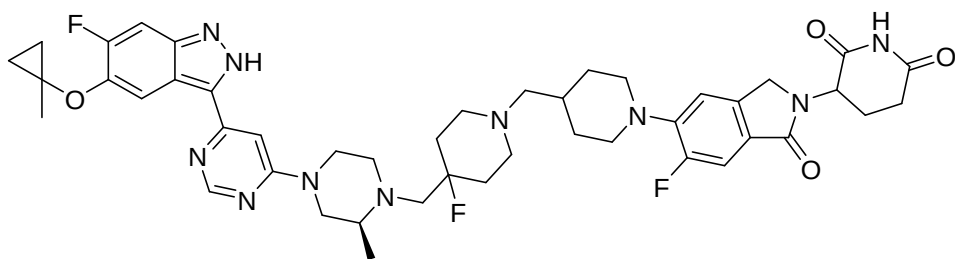
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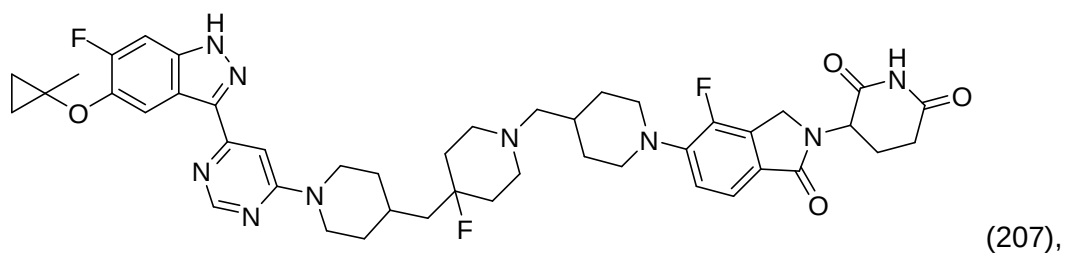
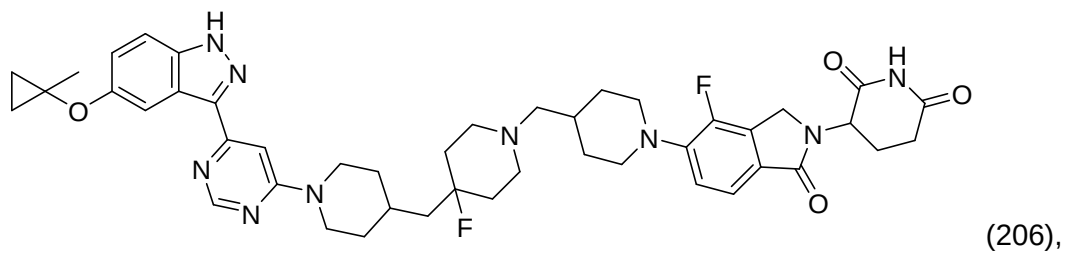
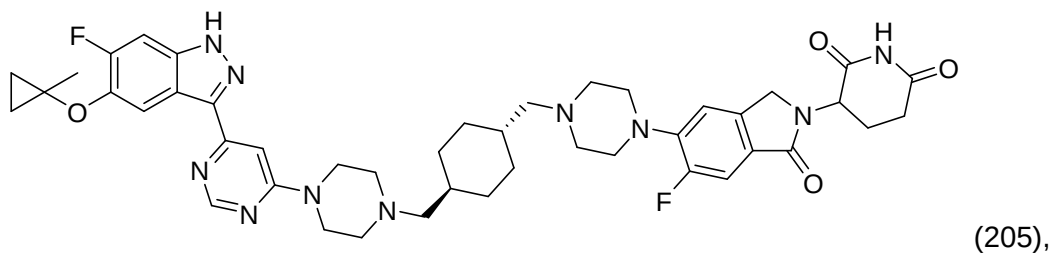
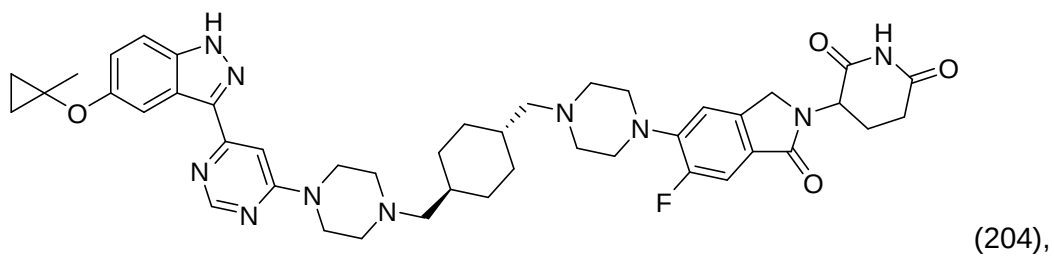
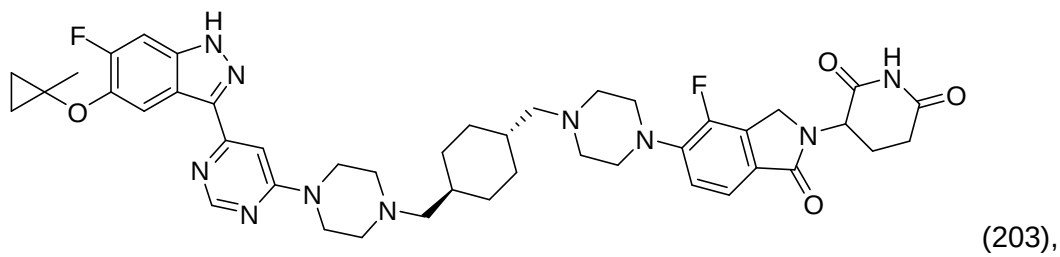
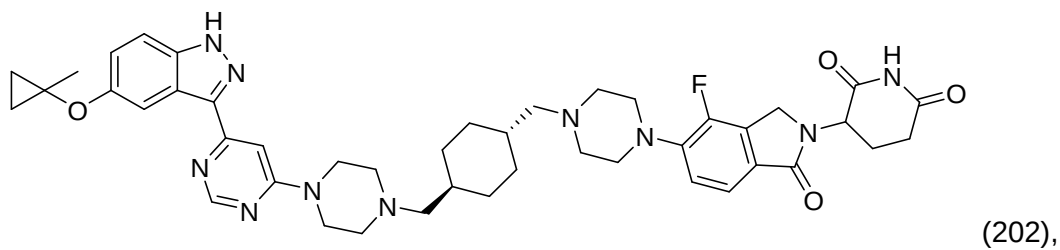


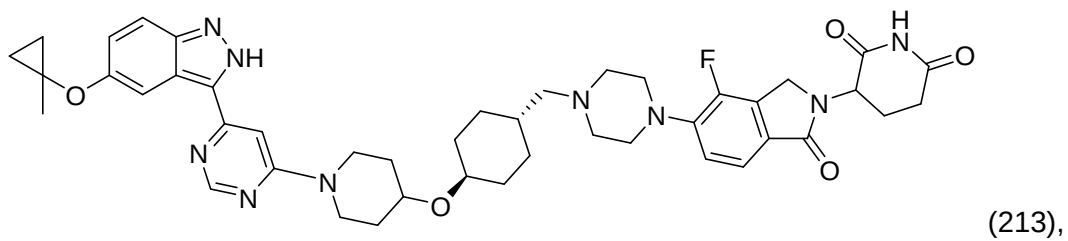
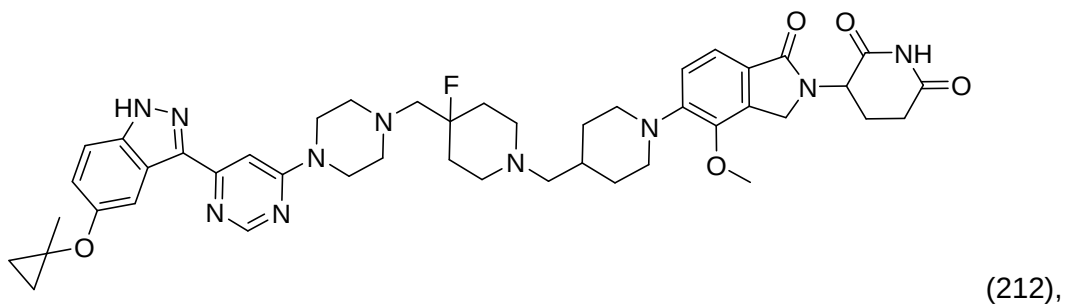
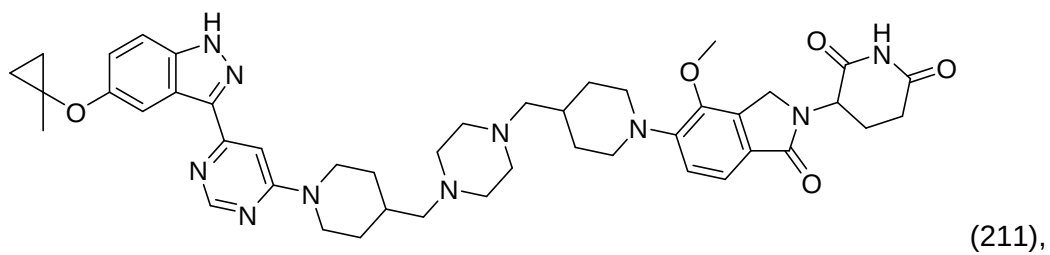
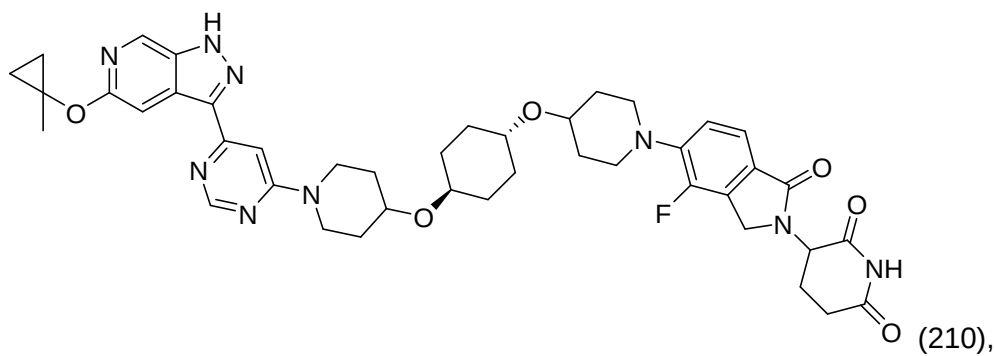
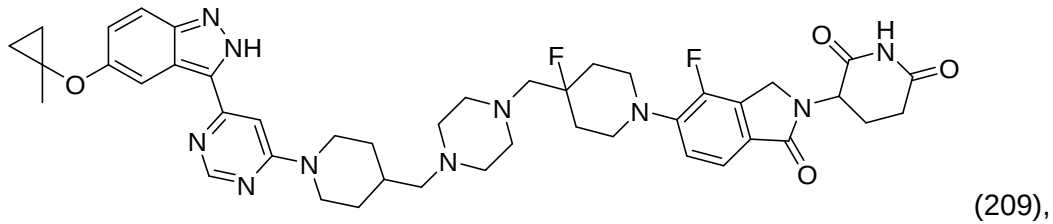
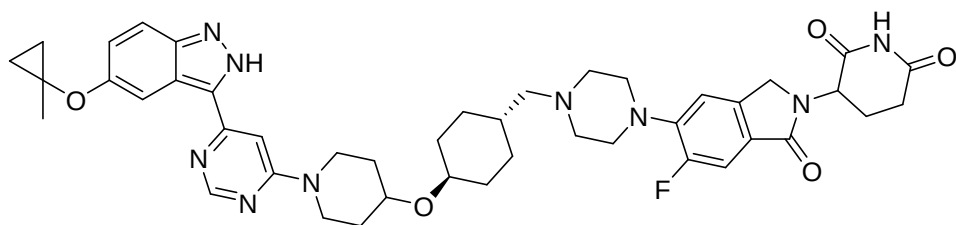
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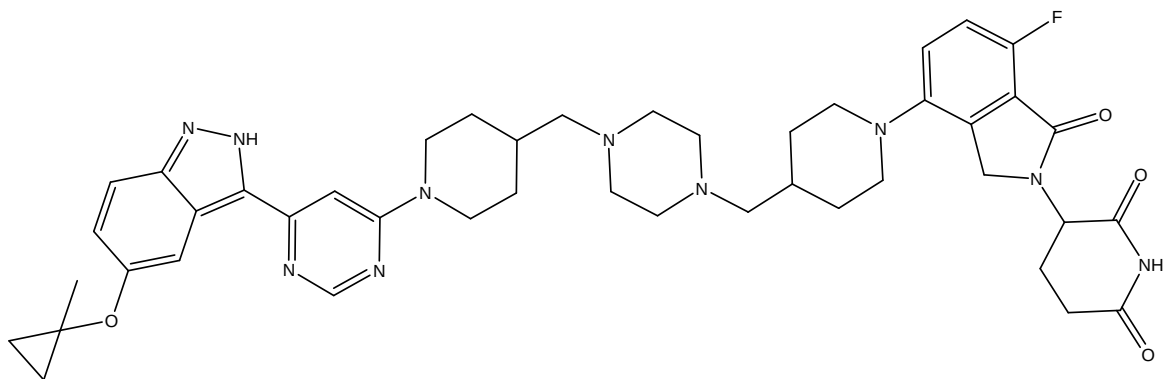




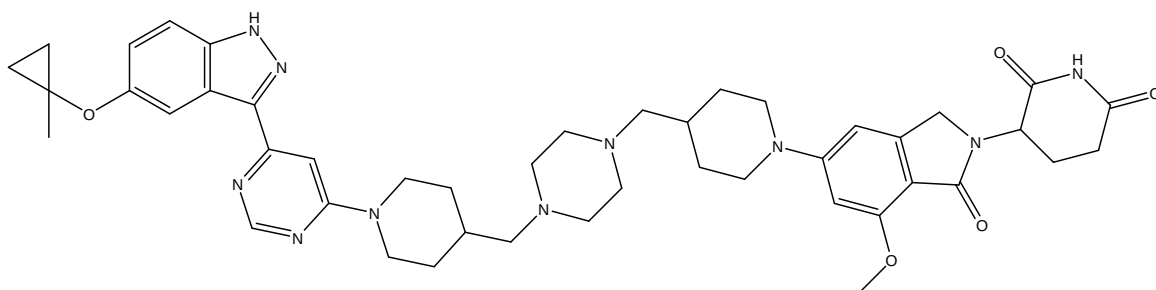




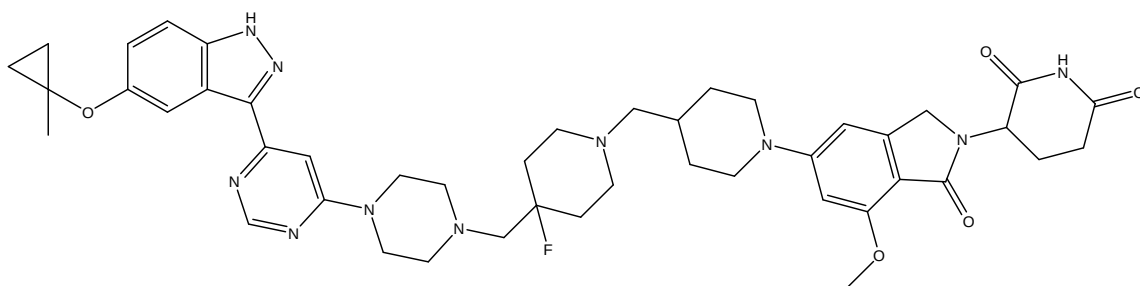




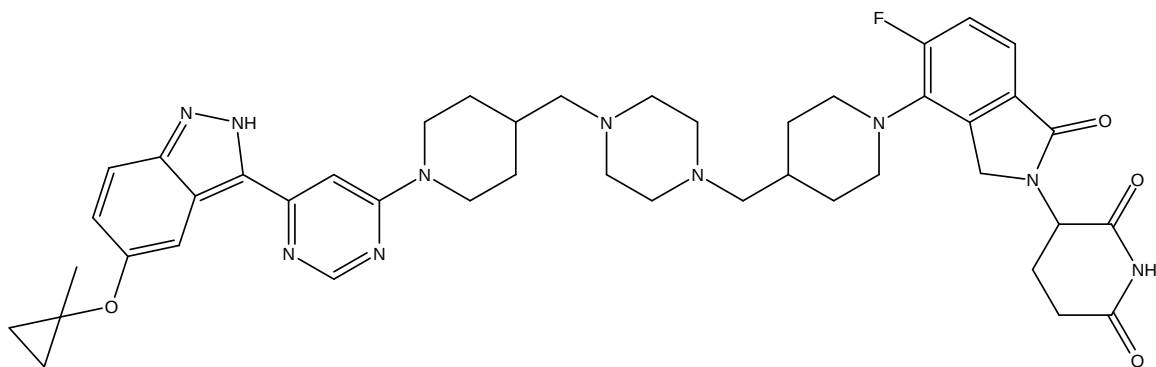
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(215),



(216),



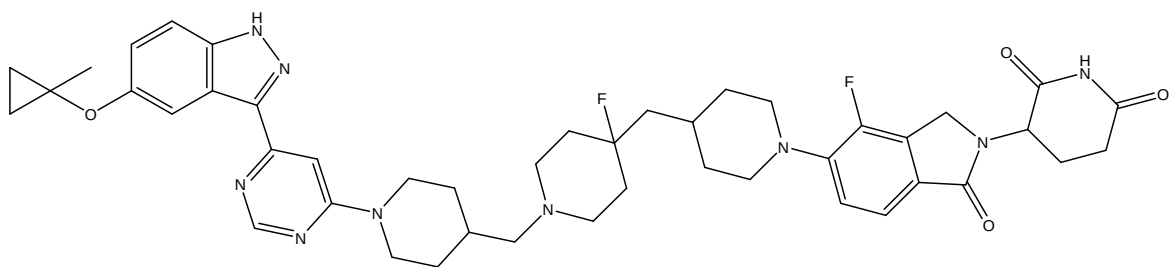
(217),

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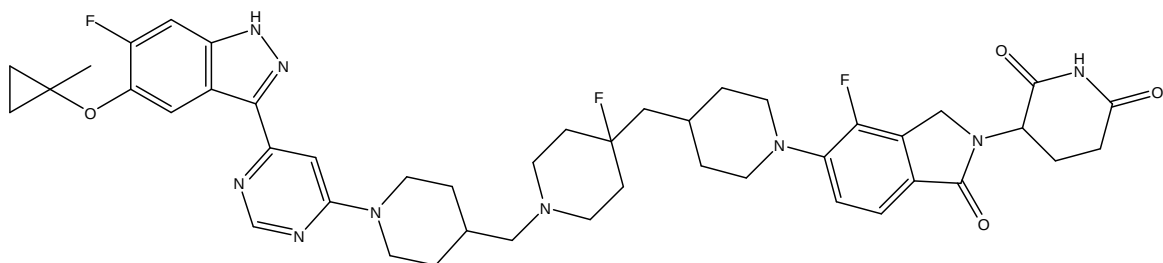
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(226),

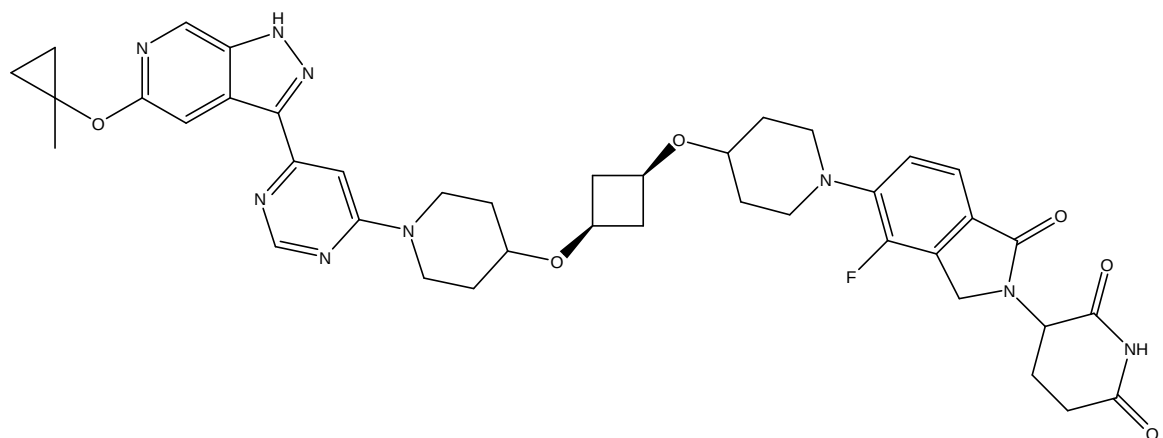
CC1(C)OC1Oc2ccc3nc4c(c3)nc5c4nc6c5nc7c6nc8c7nc9c8nc10c9nc11c10nc12c11nc13c12nc14c13nc15c14nc16c15nc17c16nc18c17nc19c18nc20c19nc21c20nc22c21nc23c22nc24c23nc25c24nc26c25nc27c26nc28c27nc29c28nc30c29nc31c30nc32c31nc33c32nc34c33nc35c34nc36c35nc37c36nc38c37nc39c38nc40c39nc41c40nc42c41nc43c42nc44c43nc45c44nc46c45nc47c46nc48c47nc49c48nc50c49nc51c50nc52c51nc53c52nc54c53nc55c54nc56c55nc57c56nc58c57nc59c58nc60c59nc61c60nc62c61nc63c62nc64c63nc65c64nc66c65nc67c66nc68c67nc69c68nc70c69nc71c70nc72c71nc73c72nc74c73nc75c74nc76c75nc77c76nc78c77nc79c78nc80c79nc81c80nc82c81nc83c82nc84c83nc85c84nc86c85nc87c86nc88c87nc89c88nc90c89nc91c90nc92c91nc93c92nc94c93nc95c94nc96c95nc97c96nc98c97nc99c98nc100c99nc101c100nc102c101nc103c102nc104c103nc105c104nc106c105nc107c106nc108c107nc109c108nc110c109nc111c110nc112c111nc113c112nc114c113nc115c114nc116c115nc117c116nc118c117nc119c118nc120c119nc121c120nc122c121nc123c122nc124c123nc125c124nc126c125nc127c126nc128c127nc129c128nc130c129nc131c130nc132c131nc133c132nc134c133nc135c134nc136c135nc137c136nc138c137nc139c138nc140c139nc141c140nc142c141nc143c142nc144c143nc145c144nc146c145nc147c146nc148c147nc149c148nc150c149nc151c150nc152c151nc153c152nc154c153nc155c154nc156c155nc157c156nc158c157nc159c158nc160c159nc161c160nc162c161nc163c162nc164c163nc165c164nc166c165nc167c166nc168c167nc169c168nc170c169nc171c170nc172c171nc173c172nc174c173nc175c174nc176c175nc177c176nc178c177nc179c178nc180c179nc181c180nc182c181nc183c182nc184c183nc185c184nc186c185nc187c186nc188c187nc189c188nc190c189nc191c190nc192c191nc193c192nc194c193nc195c194nc196c195nc197c196nc198c197nc199c198nc200c199nc201c200nc202c201nc203c202nc204c203nc205c204nc206c205nc207c206nc208c207nc209c208nc210c209nc211c210nc212c211nc213c212nc214c213nc215c214nc216c215nc217c216nc218c217nc219c218nc220c219nc221c220nc222c221nc223c222nc224c223nc225c224nc226c225nc227c226nc228c227nc229c228nc230c229nc231c230nc232c231nc233c232nc234c233nc235c234nc236c235nc237c236nc238c237nc239c238nc240c239nc241c240nc242c241nc243c242nc244c243nc245c244nc246c245nc247c246nc248c247nc249c248nc250c249nc251c250nc252c251nc253c252nc254c253nc255c254nc256c255nc257c256nc258c257nc259c258nc260c259nc261c260nc262c261nc263c262nc264c263nc265c264nc266c265nc267c266nc268c267nc269c268nc270c269nc271c270nc272c271nc273c272nc274c273nc275c274nc276c275nc277c276nc278c277nc279c278nc280c279nc281c280nc282c281nc283c282nc284c283nc285c284nc286c285nc287c286nc288c287nc289c288nc290c289nc291c290nc292c291nc293c292nc294c293nc295c294nc296c295nc297c296nc298c297nc299c298nc300c299nc301c300nc302c301nc303c302nc304c303nc305c304nc306c305nc307c306nc308c307nc309c308nc310c309nc311c310nc312c311nc313c312nc314c313nc315c314nc316c315nc317c316nc318c317nc319c318nc320c319nc321c320nc322c321nc323c322nc324c323nc325c324nc326c325nc327c326nc328c327nc329c328nc330c329nc331c330nc332c331nc333c332nc334c333nc335c334nc336c335nc337c336nc338c337nc339c338nc340c339nc341c340nc342c341nc343c342nc344c343nc345c344nc346c345nc347c346nc348c347nc349c348nc350c349nc351c350nc352c351nc353c352nc354c353nc355c354nc356c355nc357c356nc358c357nc359c358nc360c359nc361c360nc362c361nc363c362nc364c363nc365c364nc366c365nc367c366nc368c367nc369c368nc370c369nc371c370nc372c371nc373c372nc374c373nc375c374nc376c375nc377c376nc378c377nc379c378nc380c379nc381c380nc382c381nc383c382nc384c383nc385c384nc386c385nc387c386nc388c387nc389c388nc390c389nc391c390nc392c391nc393c392nc394c393nc395c394nc396c395nc397c396nc398c397nc399c398nc400c399nc401c400nc402c401nc403c402nc404c403nc405c404nc406c405nc407c406nc408c407nc409c408nc410c409nc411c410nc412c411nc413c412nc414c413nc415c414nc416c415nc417c416nc418c417nc419c418nc420c419nc421c420nc422c421nc423c422nc424c423nc425c424nc426c425nc427c426nc428c427nc429c428nc430c429nc431c430nc432c431nc433c432nc434c433nc435c434nc436c435nc437c436nc438c437nc439c438nc440c439nc441c440nc442c441nc443c442nc444c443nc445c444nc446c445nc447c446nc448c447nc449c448nc450c449nc451c450nc452c451nc453c452nc454c453nc455c454nc456c455nc457c456nc458c457nc459c458nc460c459nc461c460nc462c461nc463c462nc464c463nc465c464nc466c465nc467c466nc468c467nc469c468nc470c469nc471c470nc472c471nc473c472nc474c473nc475c474nc476c475nc477c476nc478c477nc479c478nc480c479nc481c480nc482c481nc483c482nc484c483nc485c484nc486c485nc487c486nc488c487nc489c488nc490c489nc491c490nc492c491nc493c492nc494c493nc495c494nc496c495nc497c496nc498c497nc499c498nc500c499nc501c500nc502c501nc503c502nc504c503nc505c504nc506c505nc507c506nc508c507nc509c508nc510c509nc511c510nc512c511nc513c512nc514c513nc515c514nc516c515nc517c516nc518c517nc519c518nc520c519nc521c520nc522c521nc523c522nc524c523nc525c524nc526c525nc527c526nc528c527nc529c528nc530c529nc531c530nc532c531nc533c532nc534c533nc535c534nc536c535nc537c536nc538c537nc539c53CC1(C)OC1c2cc(F)c3c2c[nH]3-c4ncnc4N5CCN(CC5)CCN6CCN(CC6)CC(F)N7CCN(C7)c8cc(F)c9c8c(=O)n(c9=O)C10CCCC(=O)N10CC1(C)OC1c2ccc3c(c2)c4nn[nH]4-c5ncnc5N6CCN(CC6)CCN7C8CCN(CC8)CC7Cc9ccccc9N10C(=O)CNC10=O



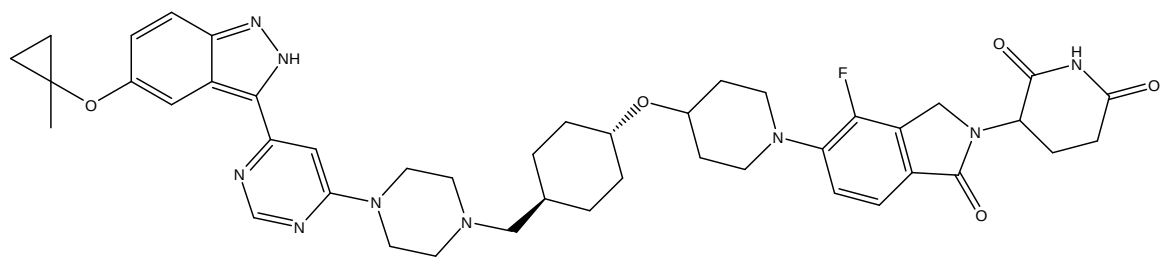
(231),



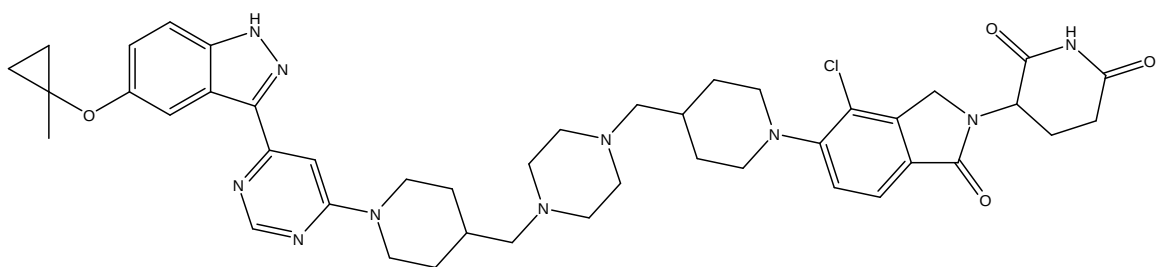
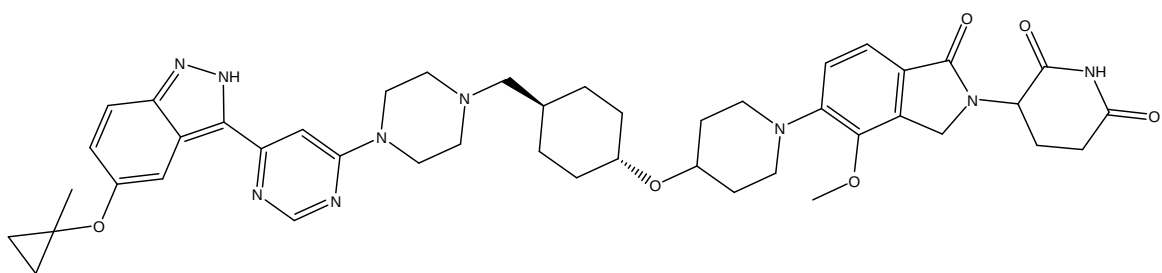
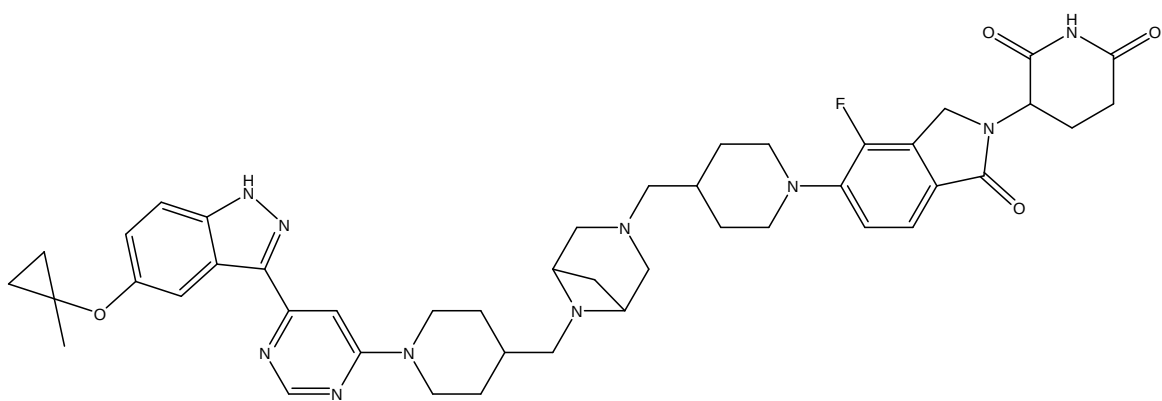
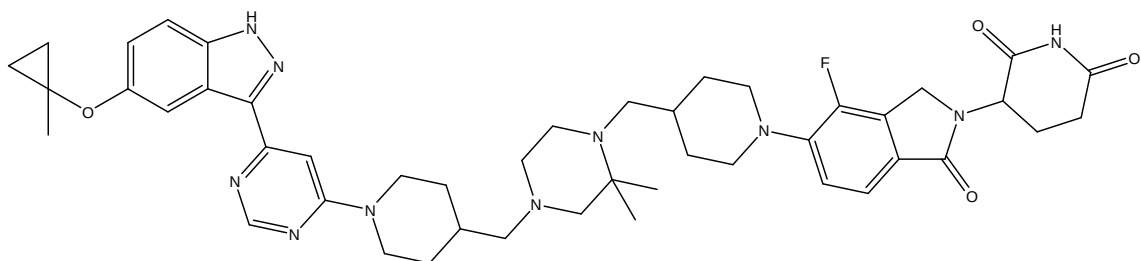
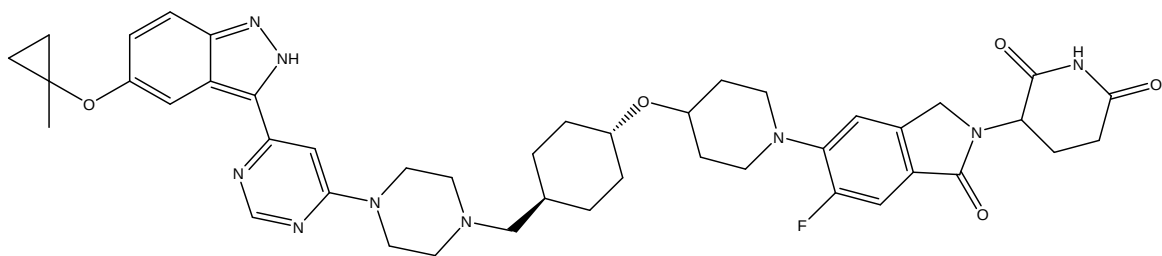
(232),

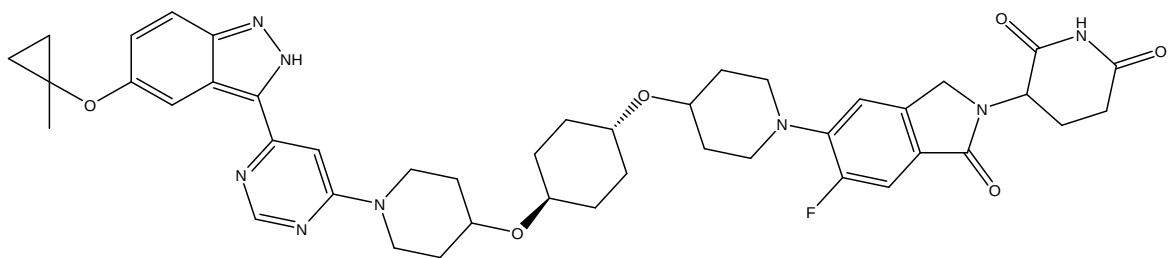


(233),

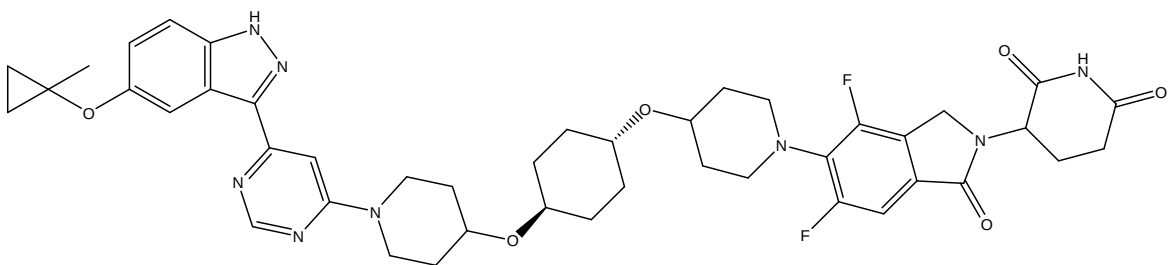


(234),

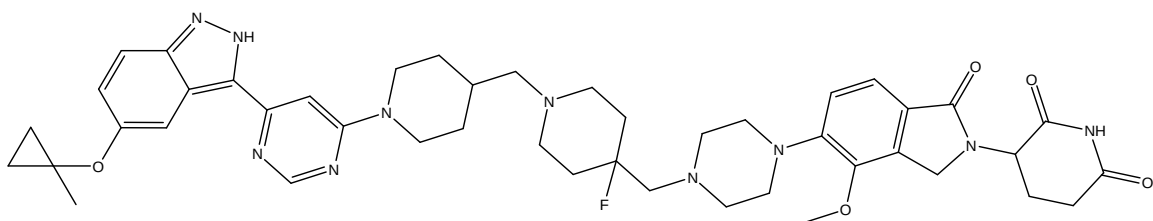




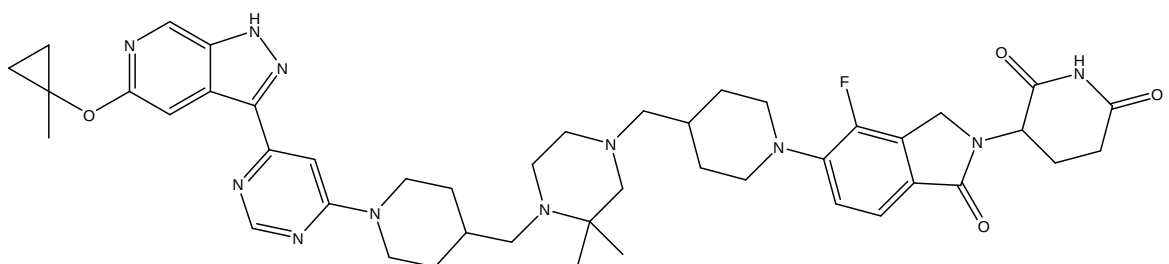
(244),



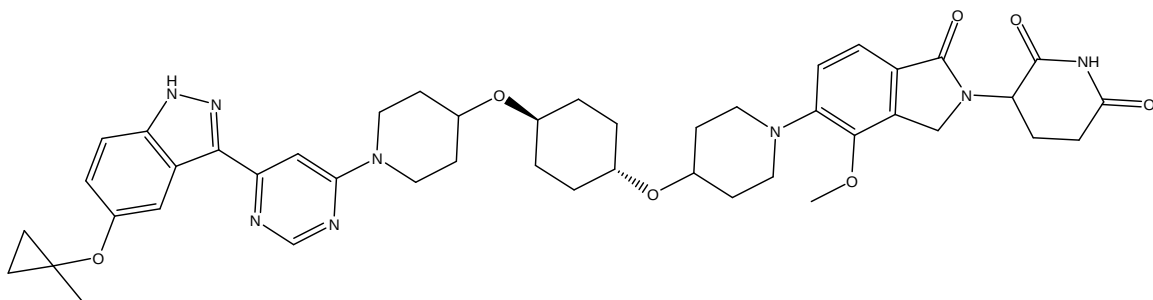
(245),



(246),



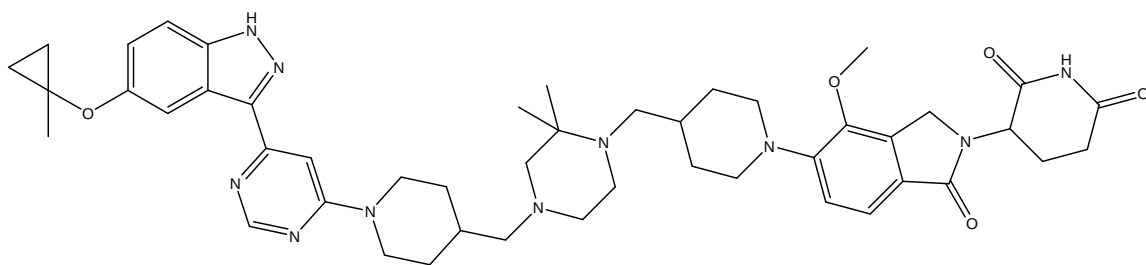
(247),



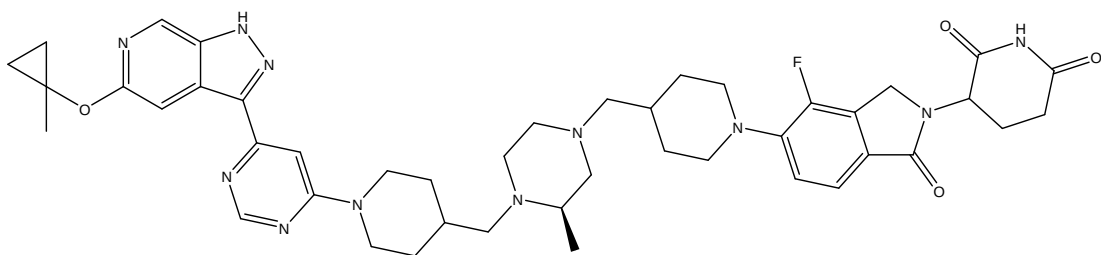
(248),

CC1(C)CCN(C1)CCN2C(C(C2)C)CCN3CCCCN3CCN4C(=O)C(=O)NCC5=C4C(=O)C6=CC=C(C=C5OC)N(C6)CCN7CCCCN7CCN8C=NC9=C(N8)C(=C(C=C9)C10=CC=CC=C10OC11CCOC11)N2CN1C(=O)CCc2cc(O)c3ccc(NC4CCCCC4CN(C5CCCCC5)CC6CCCCC6N7CCCCC7C8=NC9=C(N=CN=C8C9=CC=C10OC11CC2CC2CC11)N3)cc2CC1(C)OC1c2ccc3c(c2)c4[nH]cnc4c5c3ncnc5N6CCCCC6Oc7c8ccccc8c(c7)C9CCN(CCN9C10C=CC(=O)N10)c12cc(OC)c3c(c12)c(=O)[nH]c3=O

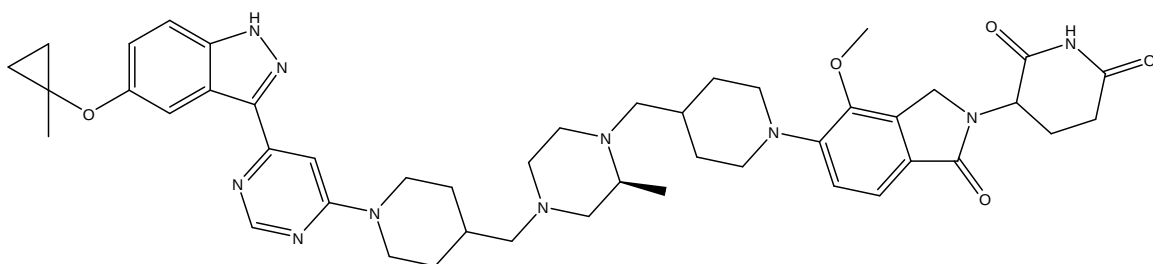
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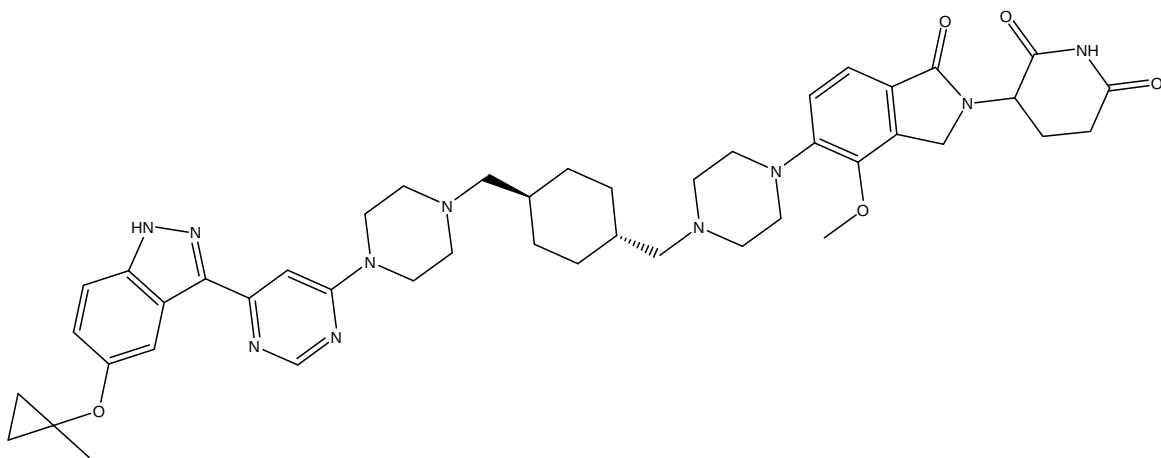
(262),



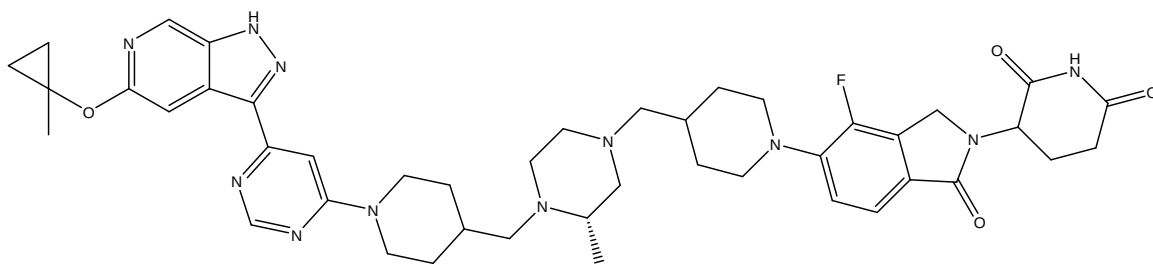
(263),



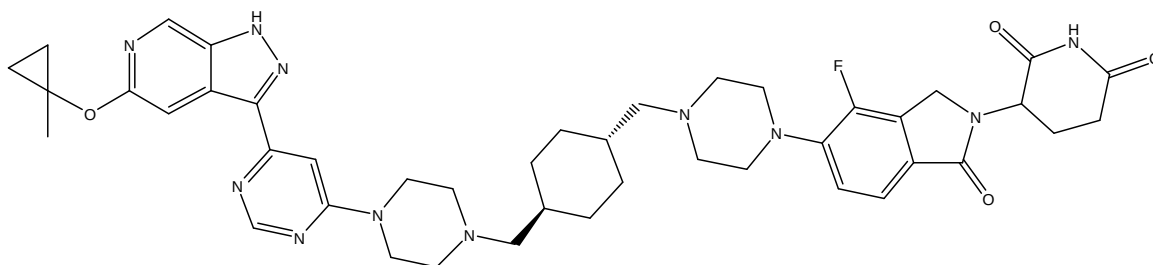
(264),



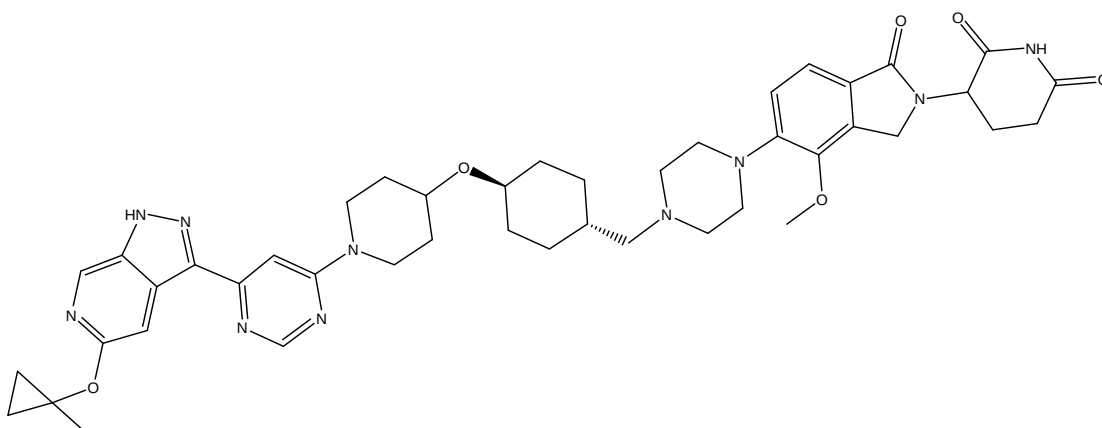
(265),



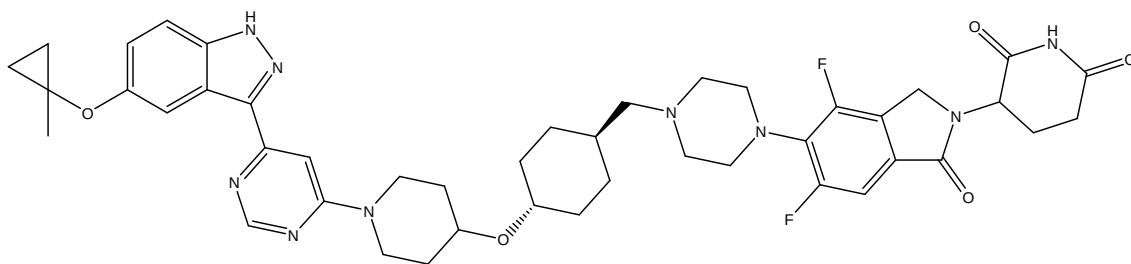
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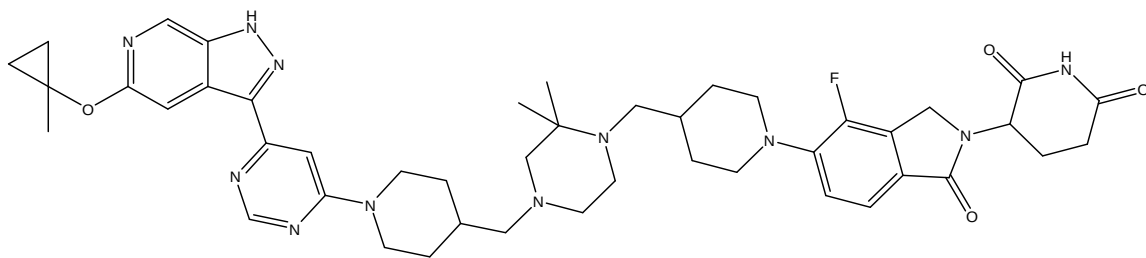
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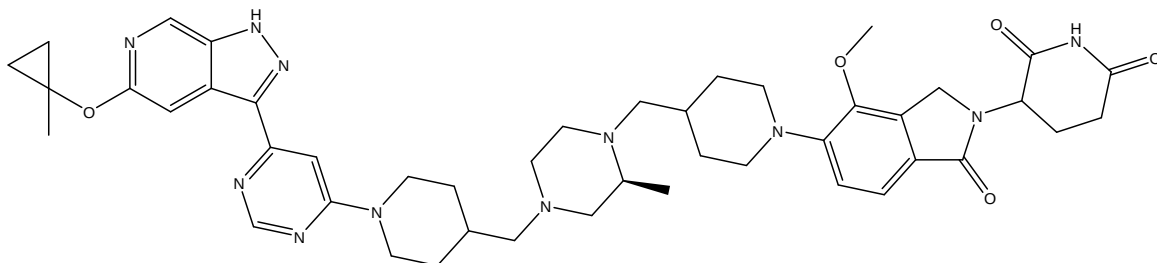
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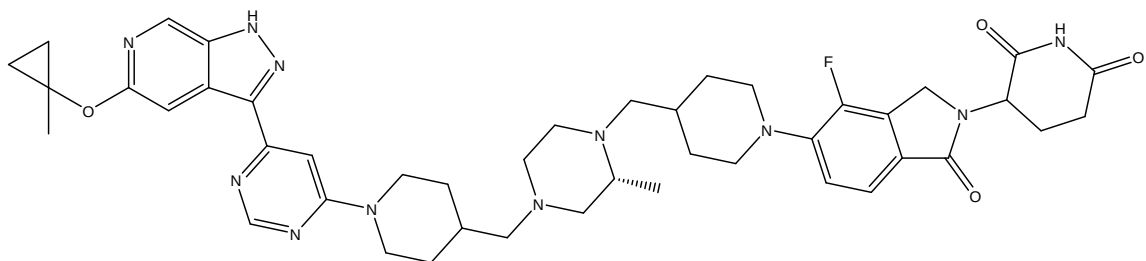
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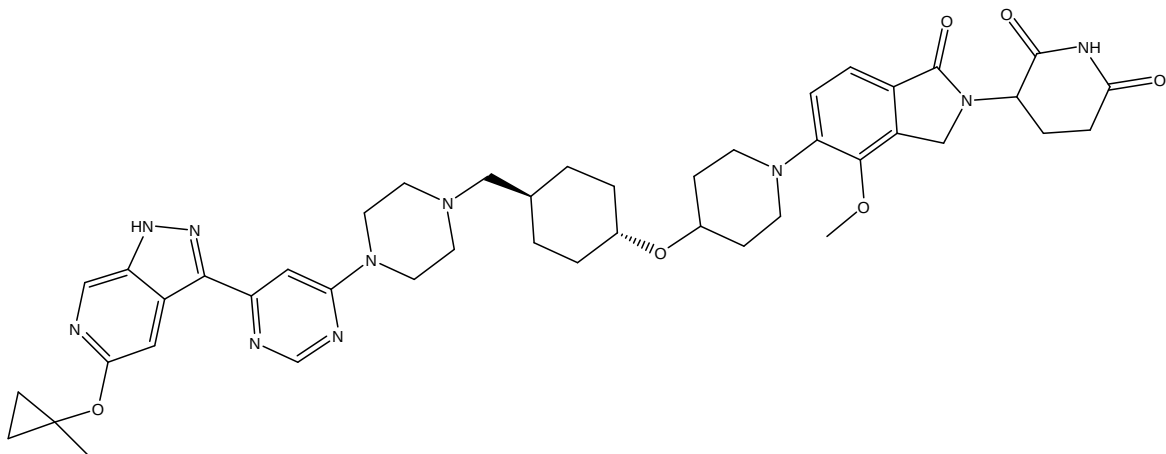
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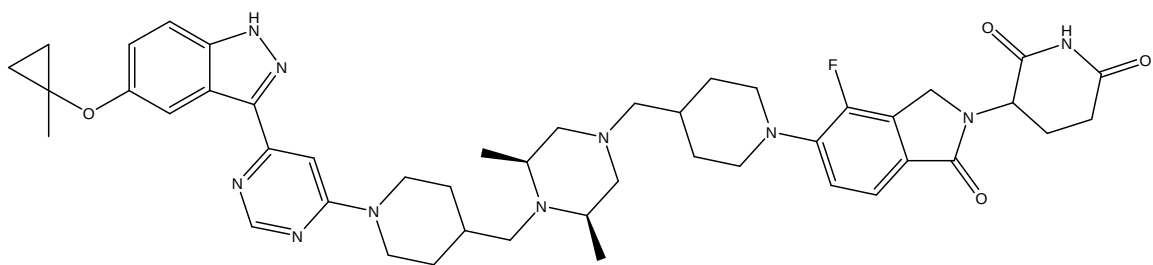


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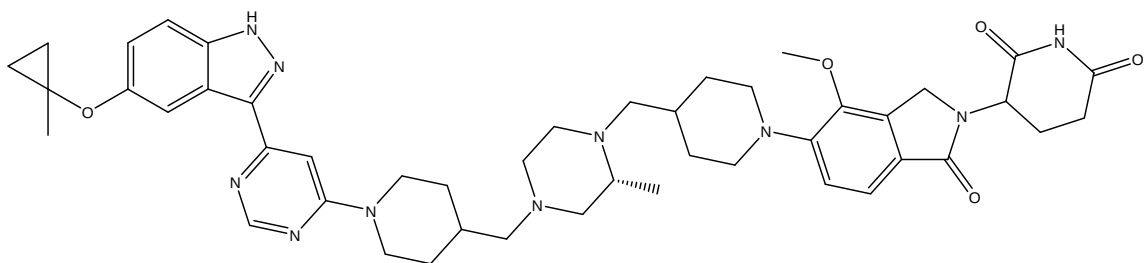
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(278),

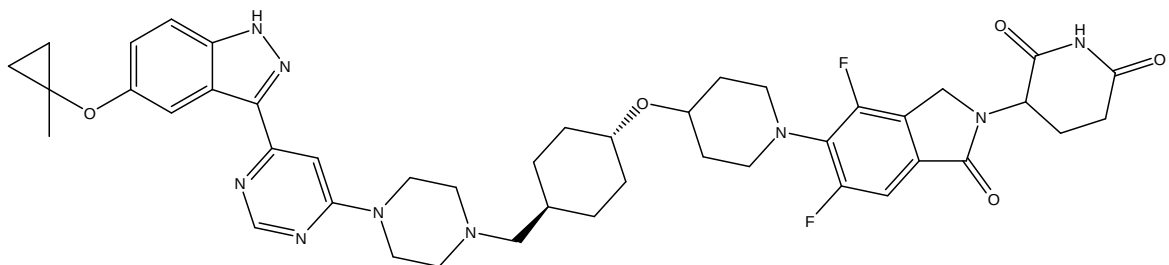
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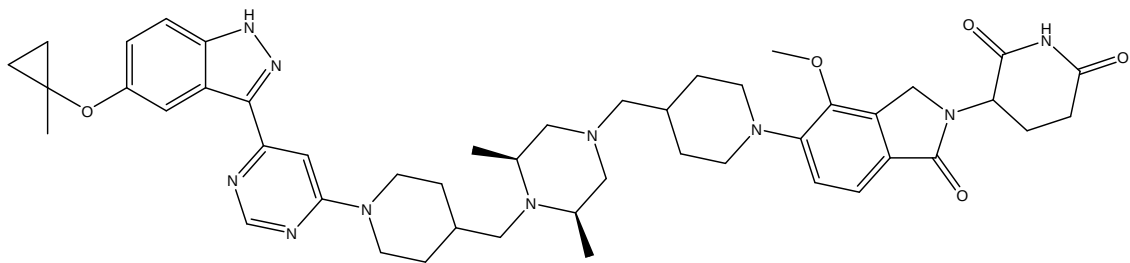
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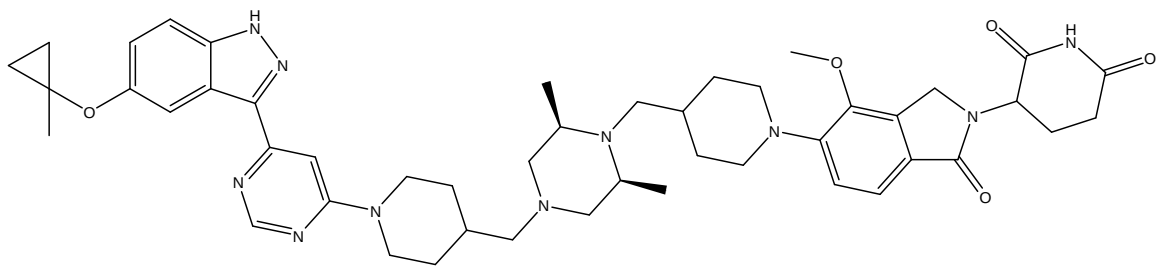
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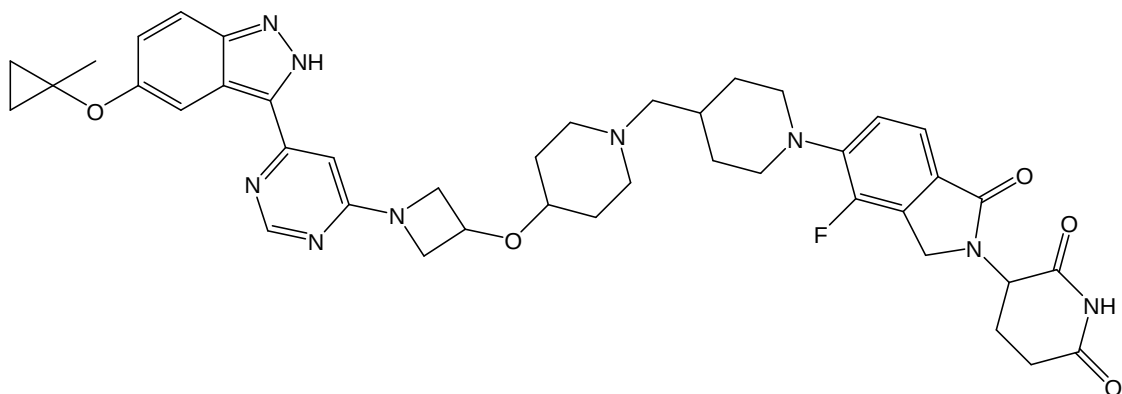
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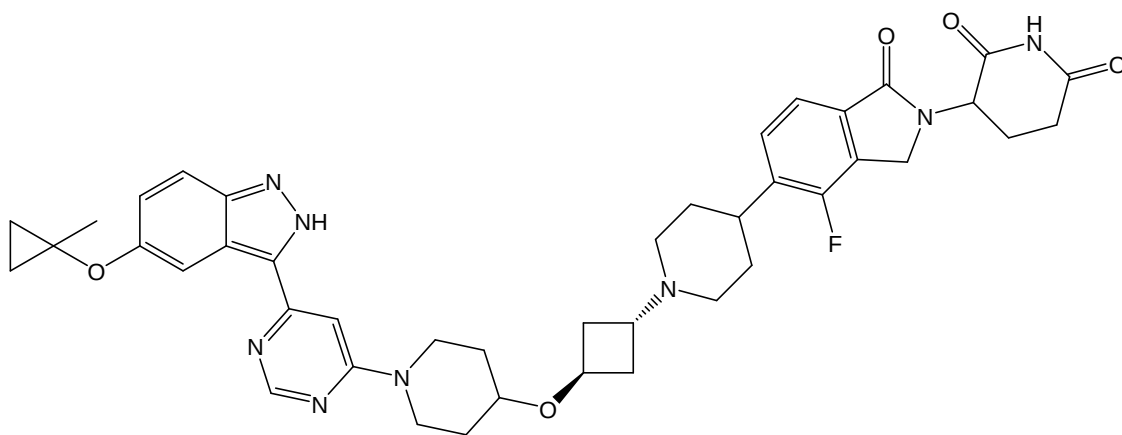
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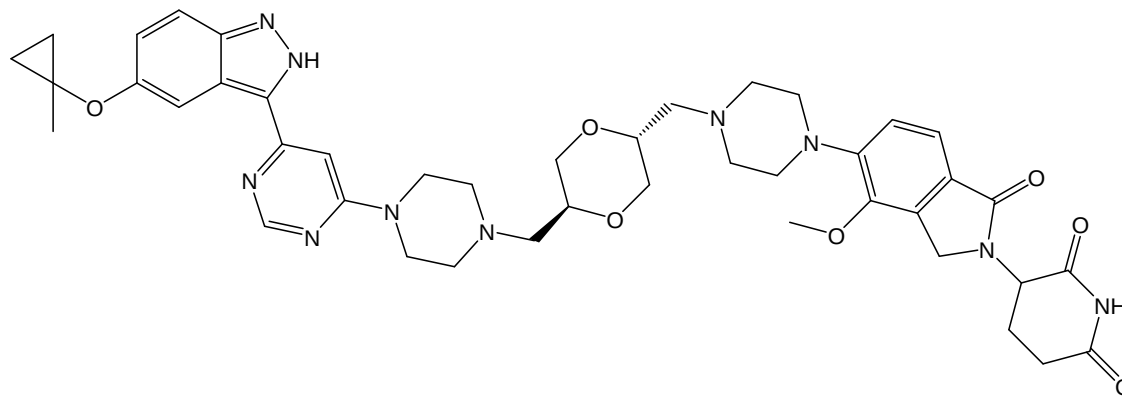
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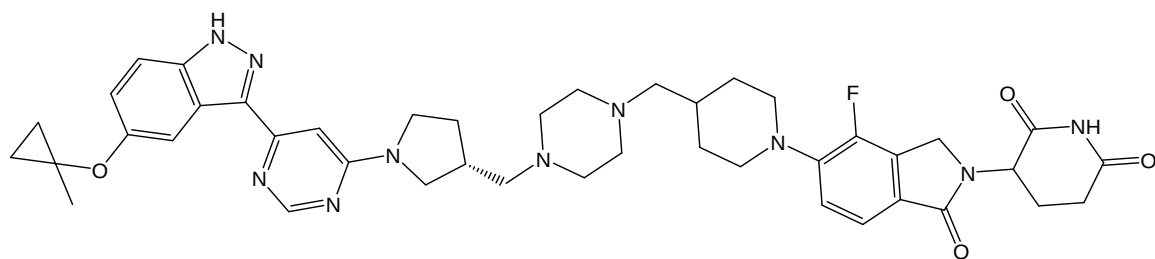
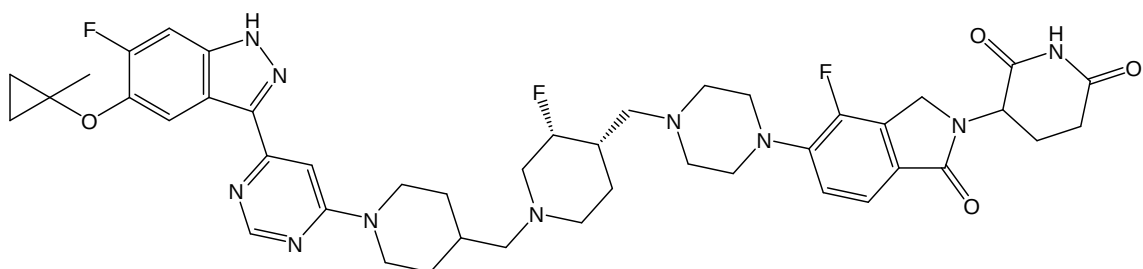
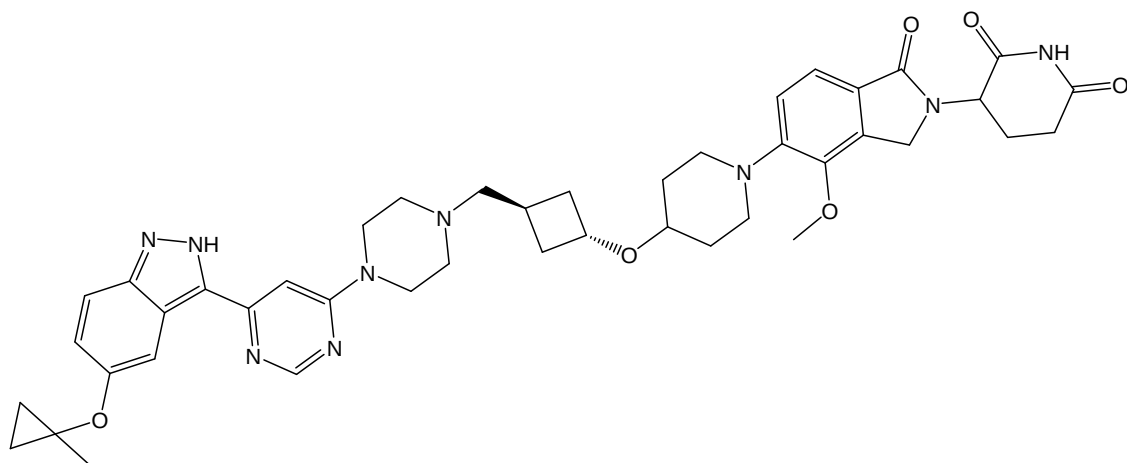
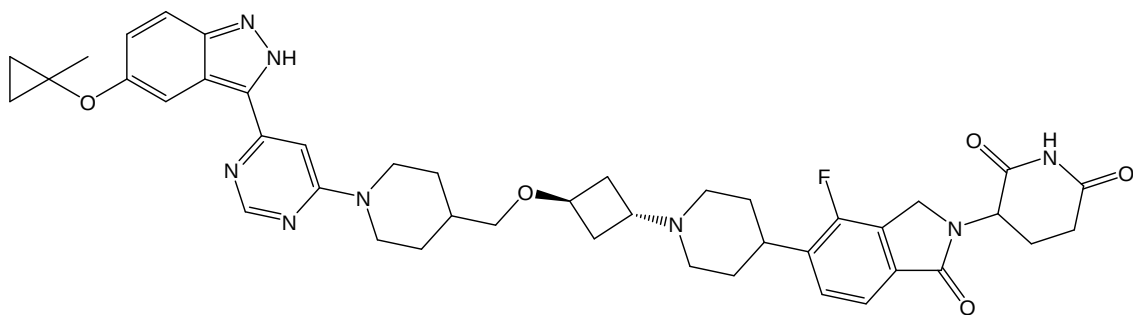
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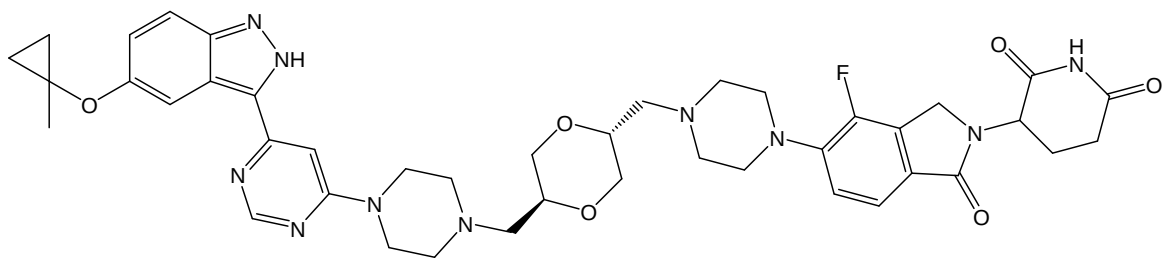


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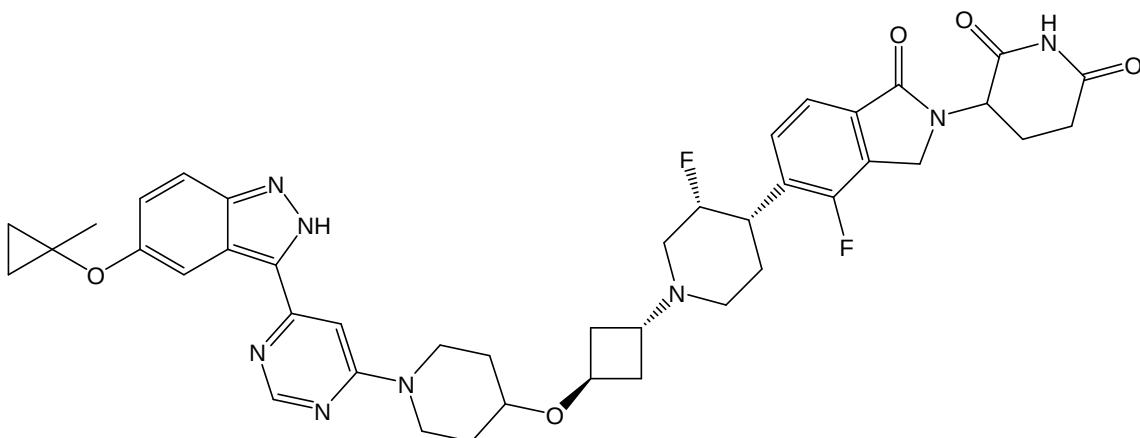


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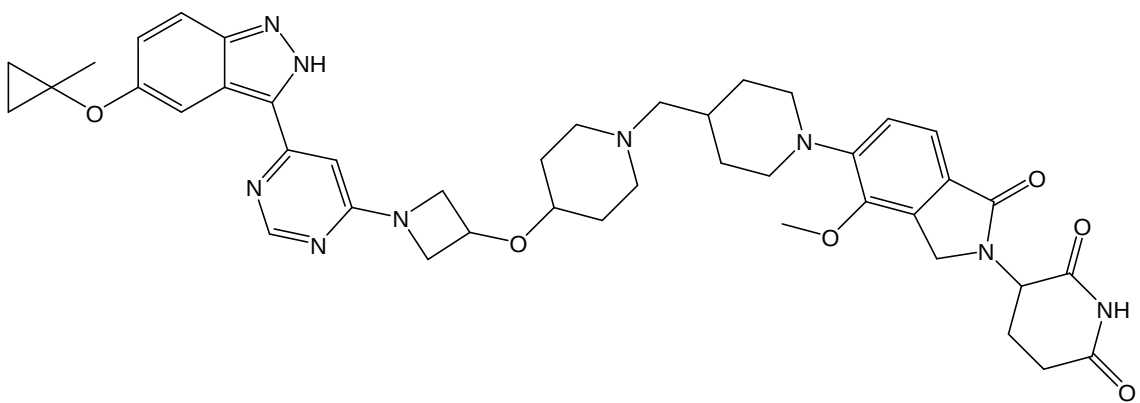




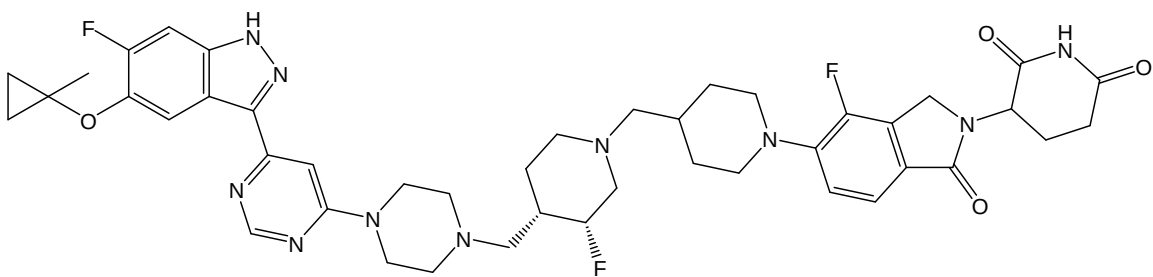
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(297),



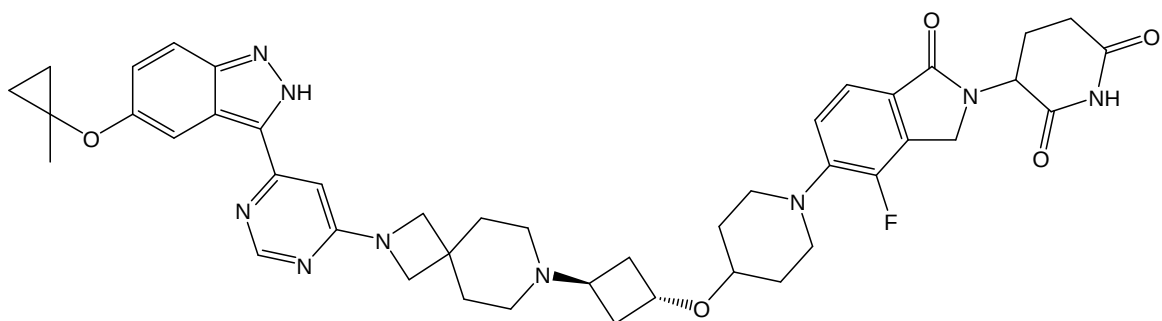
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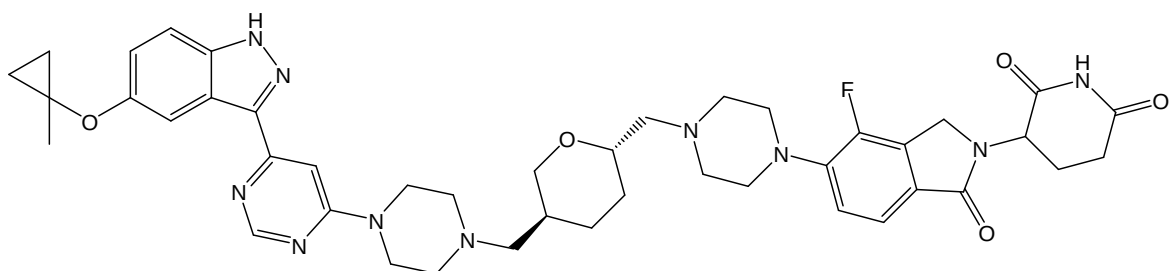
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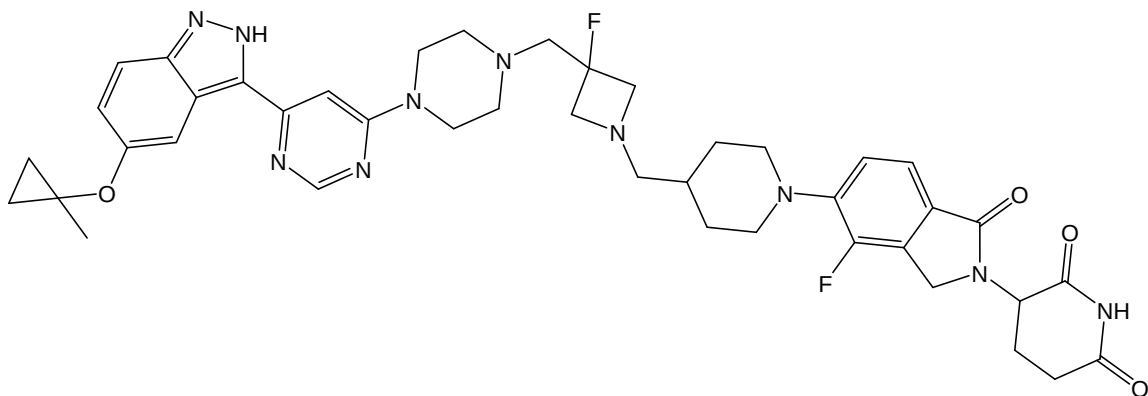
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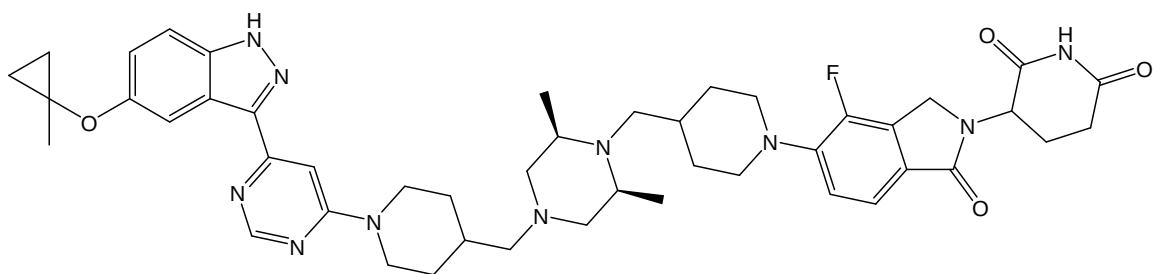
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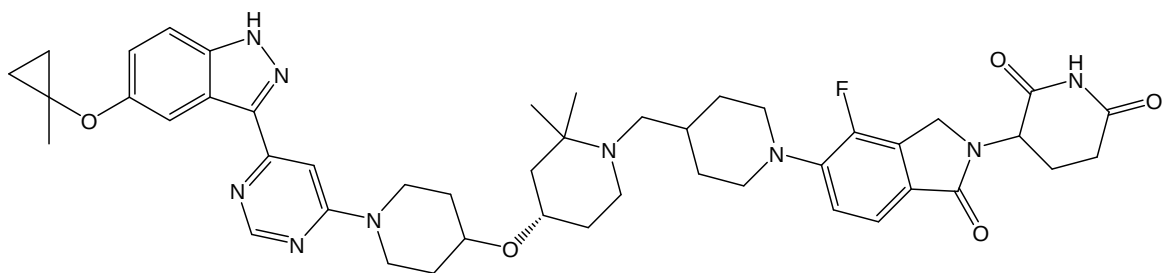
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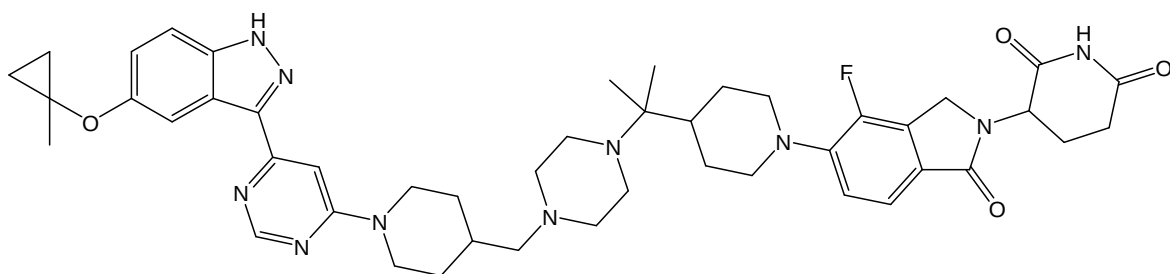
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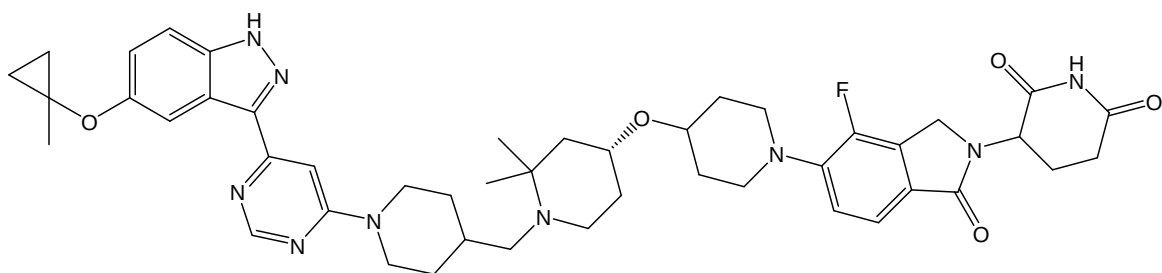
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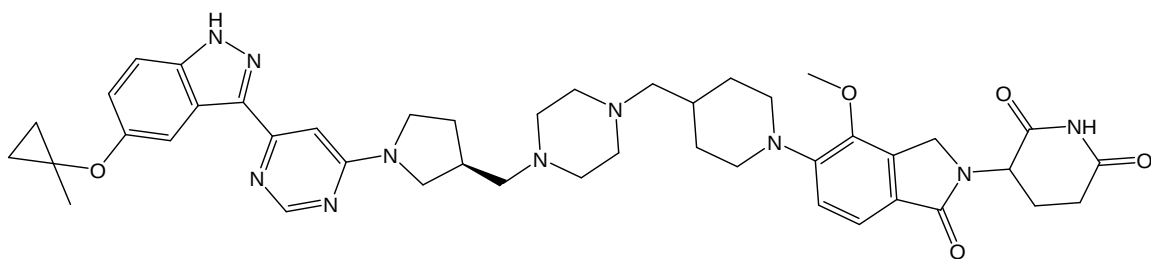
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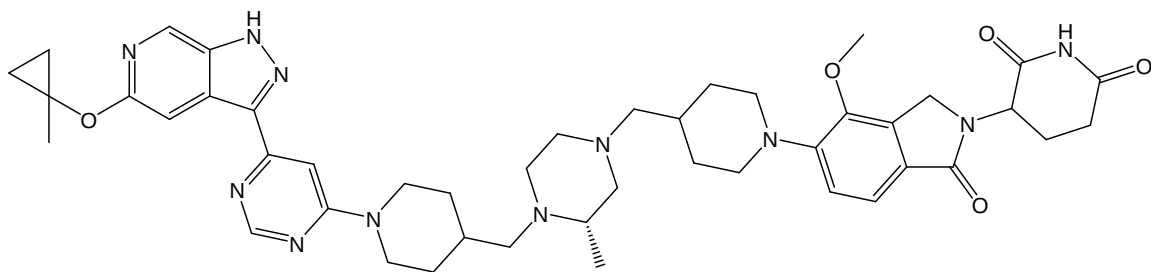
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(310),



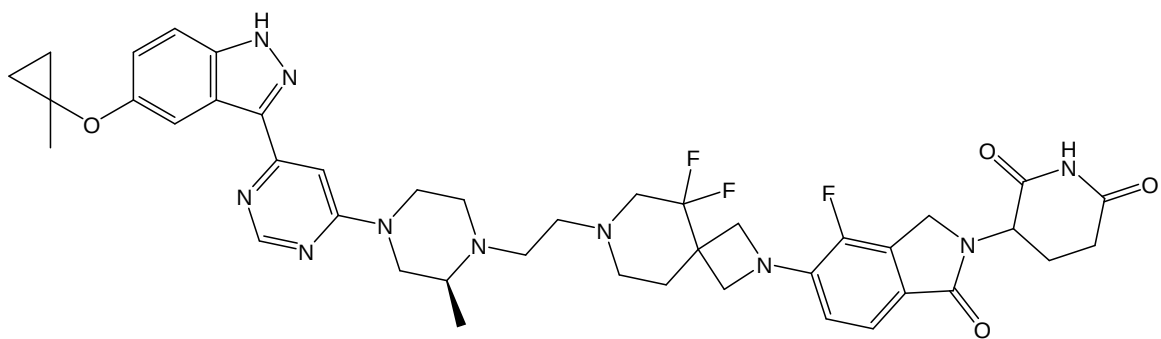
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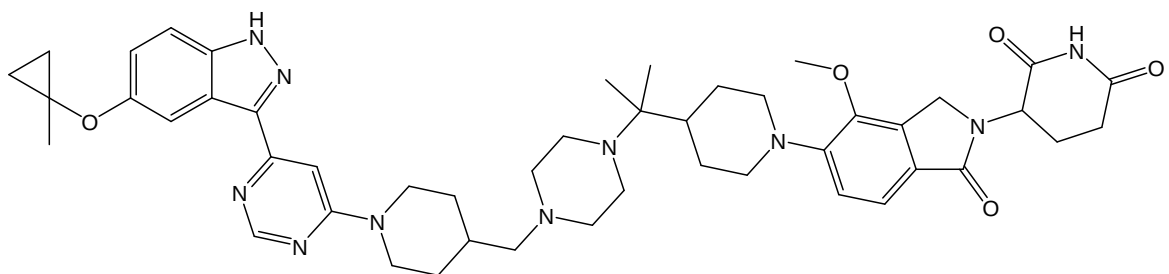
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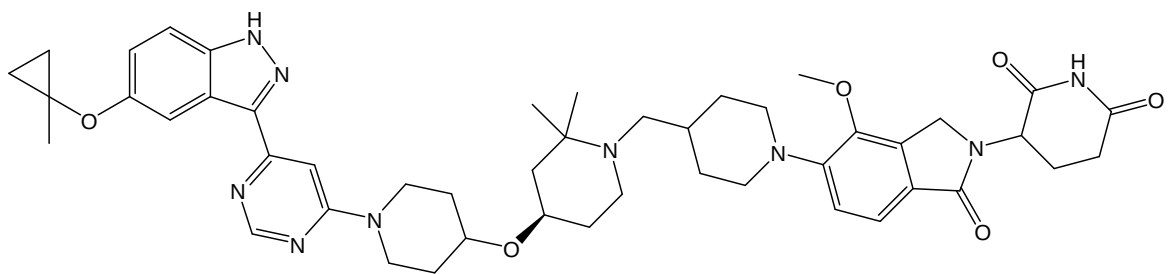
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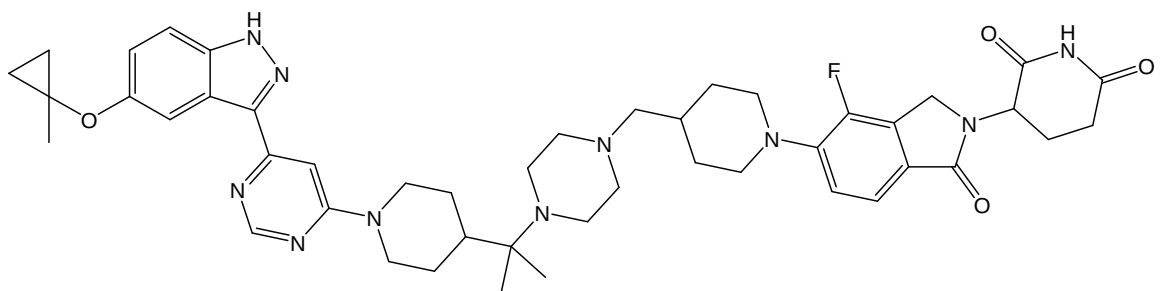
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(318),



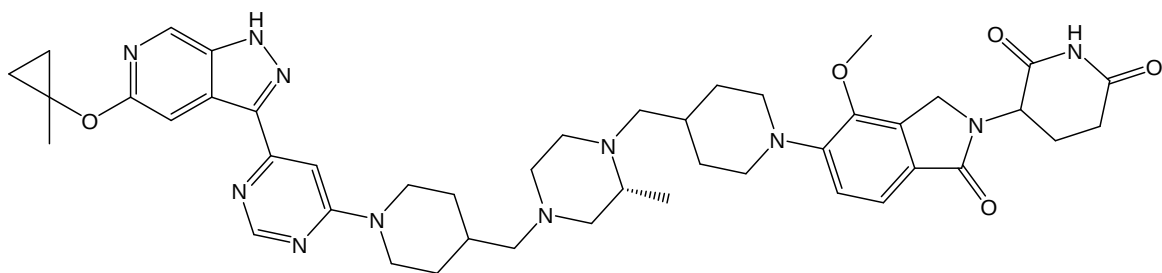
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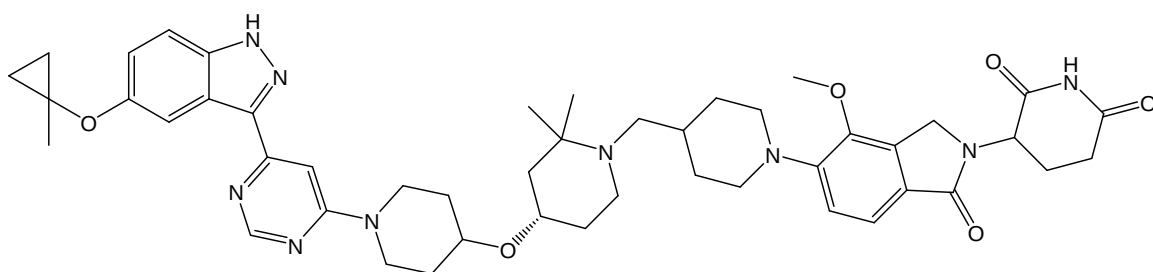
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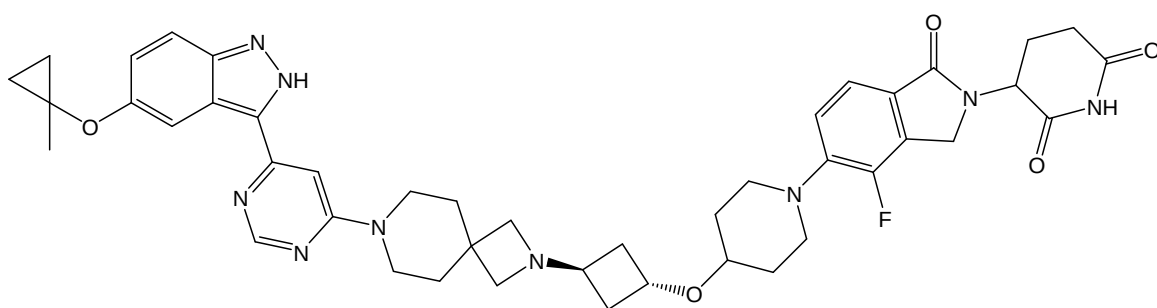
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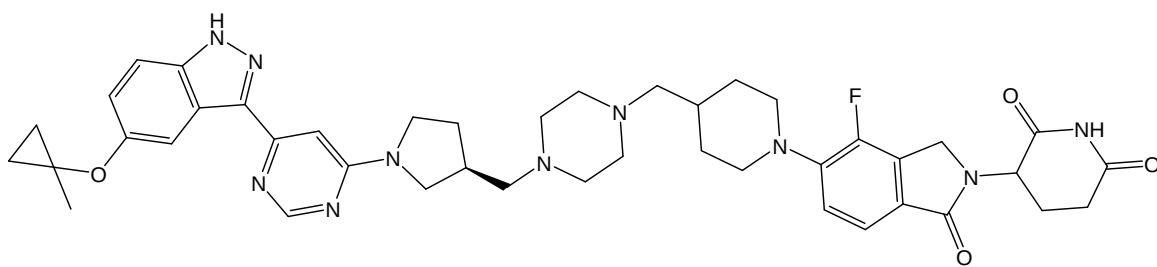
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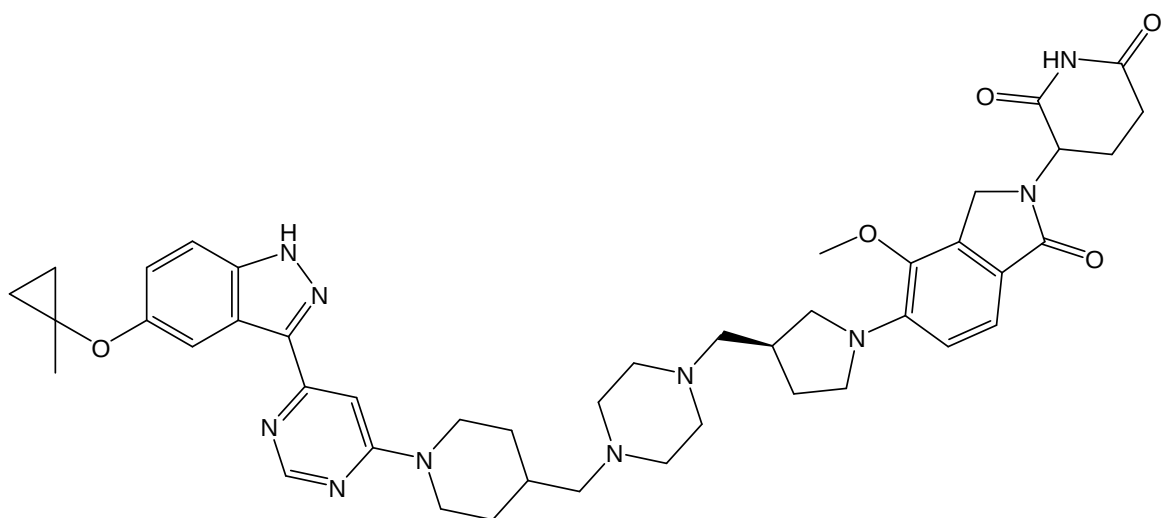
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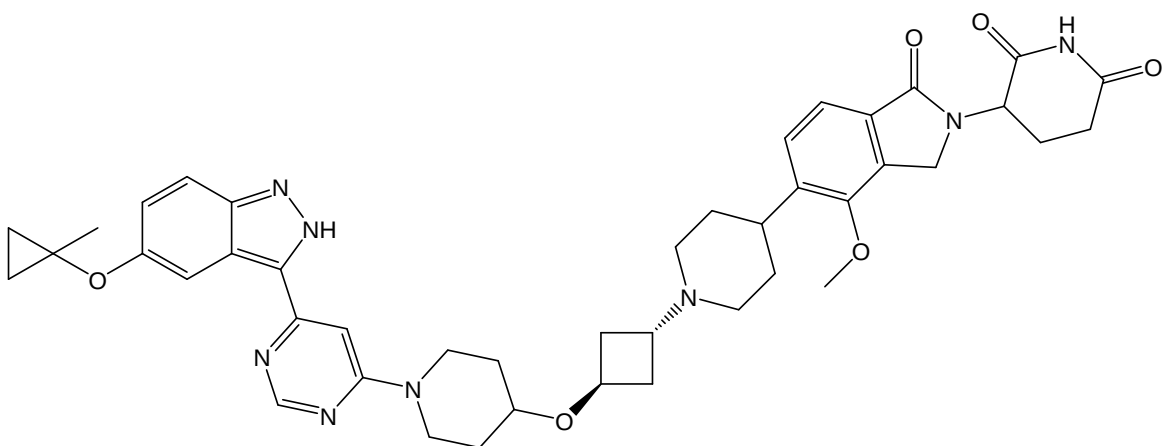
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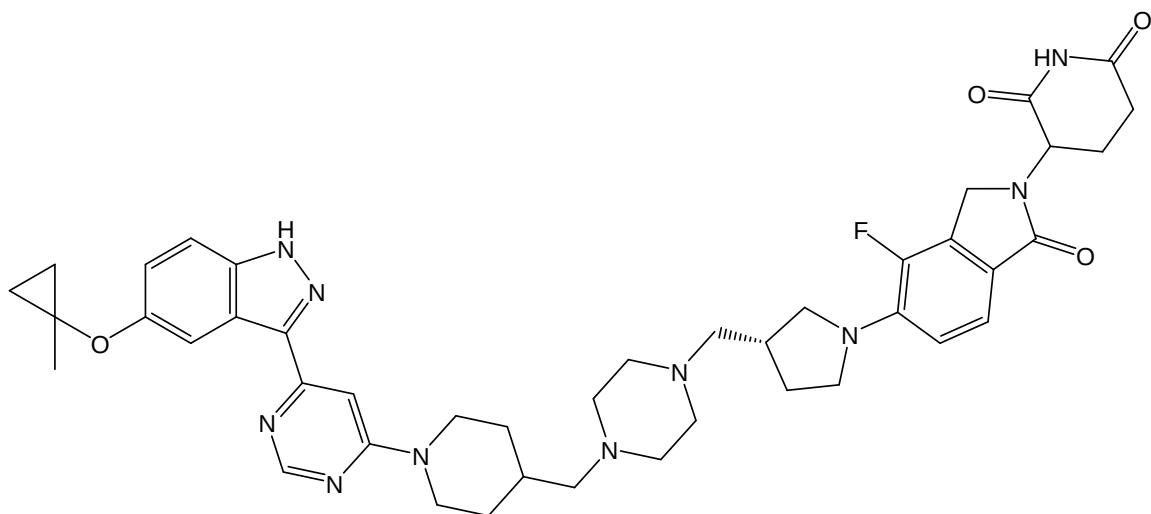
(327),



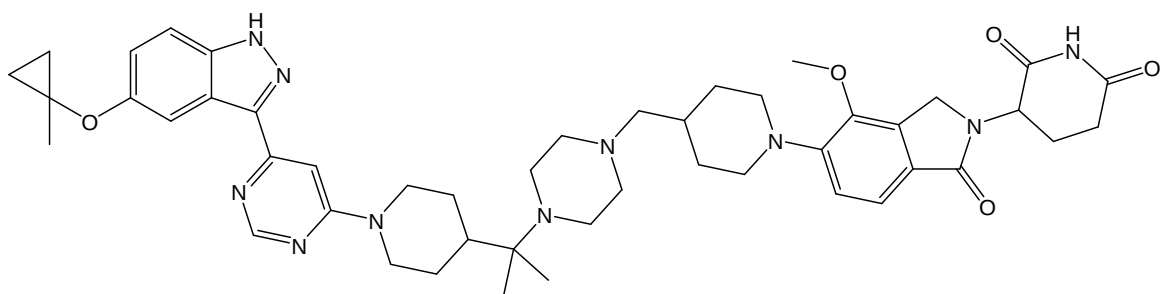
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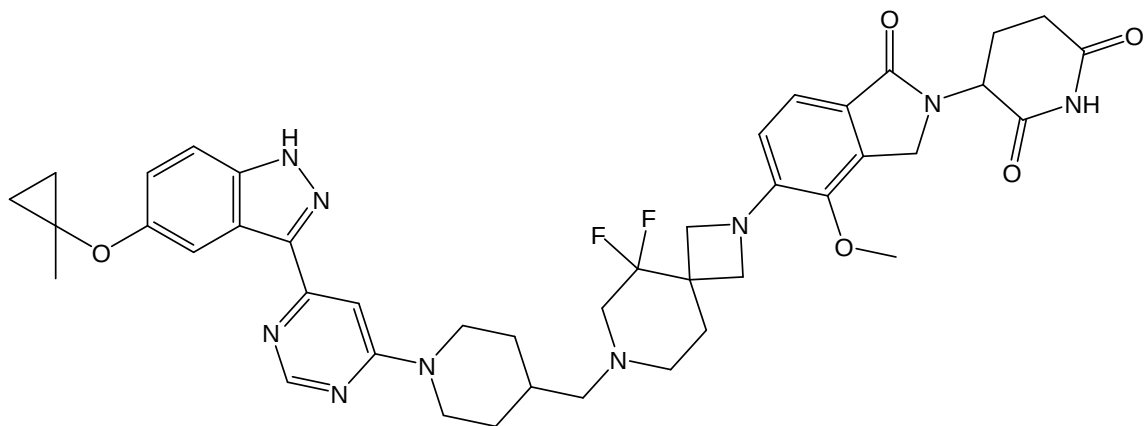
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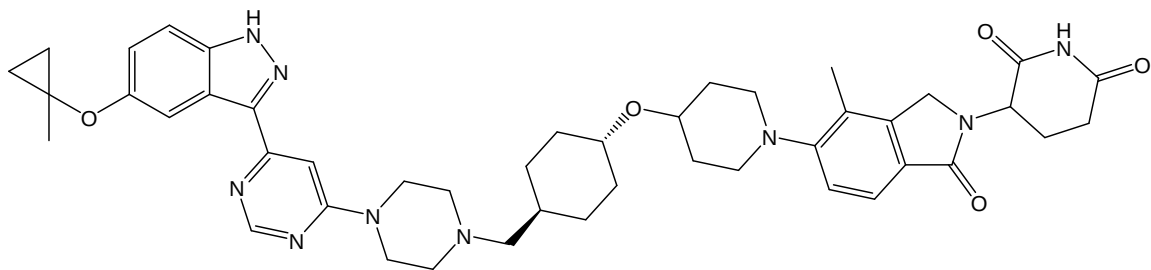
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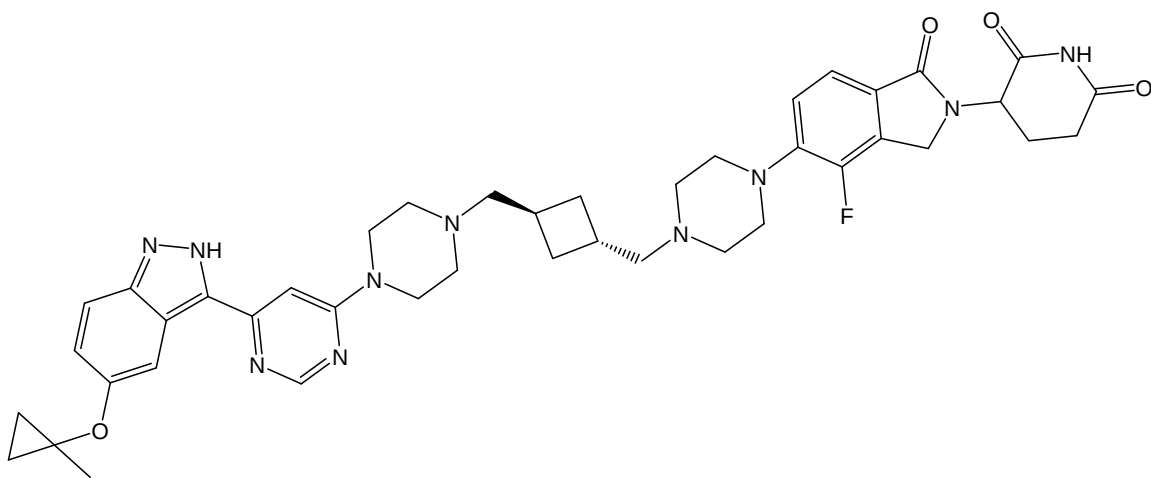
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(332),



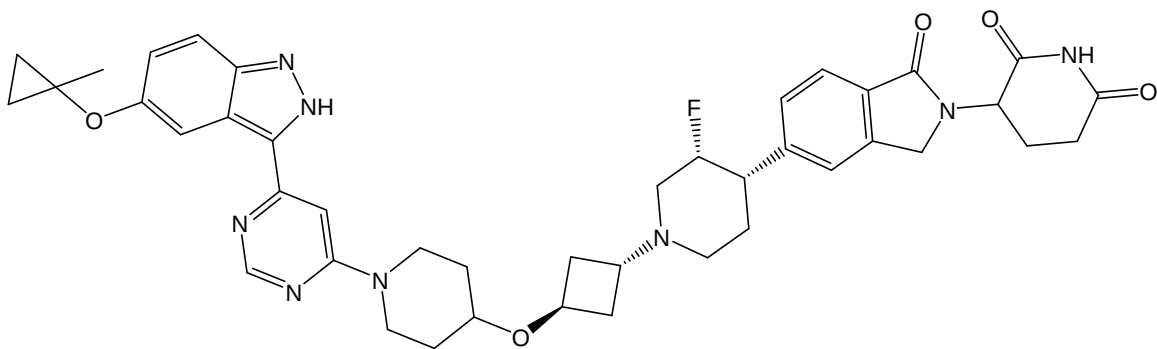
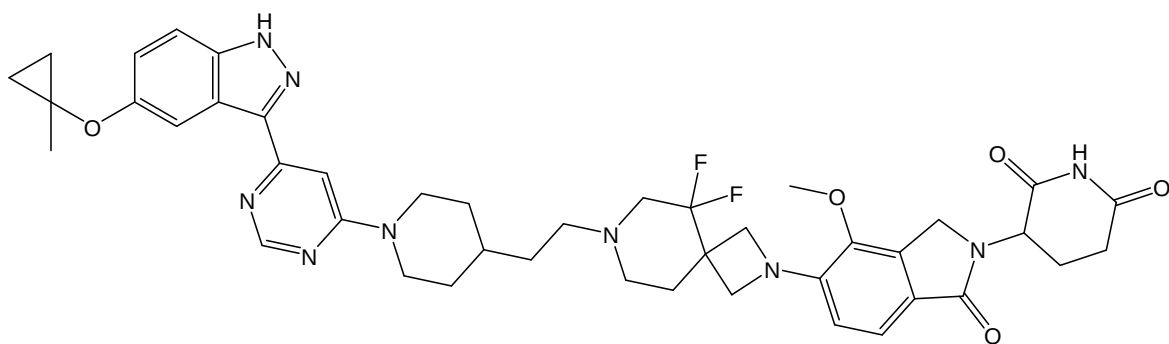
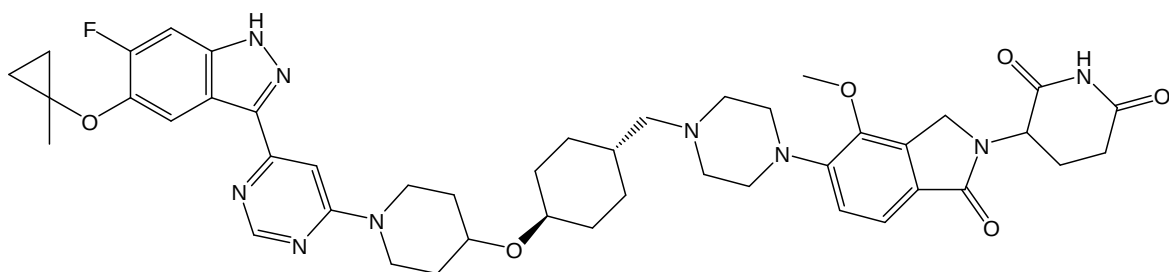
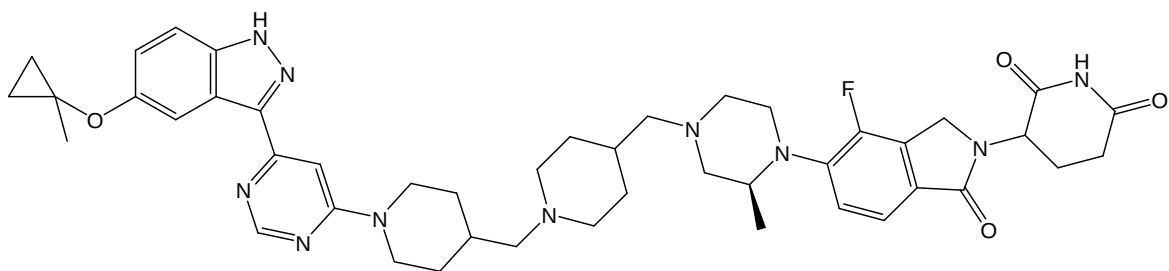
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(334),

CC1(C)OC2=CC=C3C(=C2)N=NC3=C4N=CN=C4N5CCN(CCN5CCN6C(F)(F)C7CCN(C7C6)c8ccc9c8c(=O)nc(=O)cc9=O)c9ccccc9FCC1(C)CO1c2ccc3c(c2)c[nH]3c4ncnc5c4nnc5N6CCCCC6CN7C(F)CC8CCCCN8c9cc(F)c10c(c9)c(=O)[nH]c10=OCC1(C)CCN(C1)CCN2C(C(C)(C)N2)CCN3CCN(C3)CCN4C(=O)C(=O)NCC4c5ccc(OC)c(N6CCN(C6)Cc7ccc8c5cnc8c7OC9C1CC9)c7

(338),

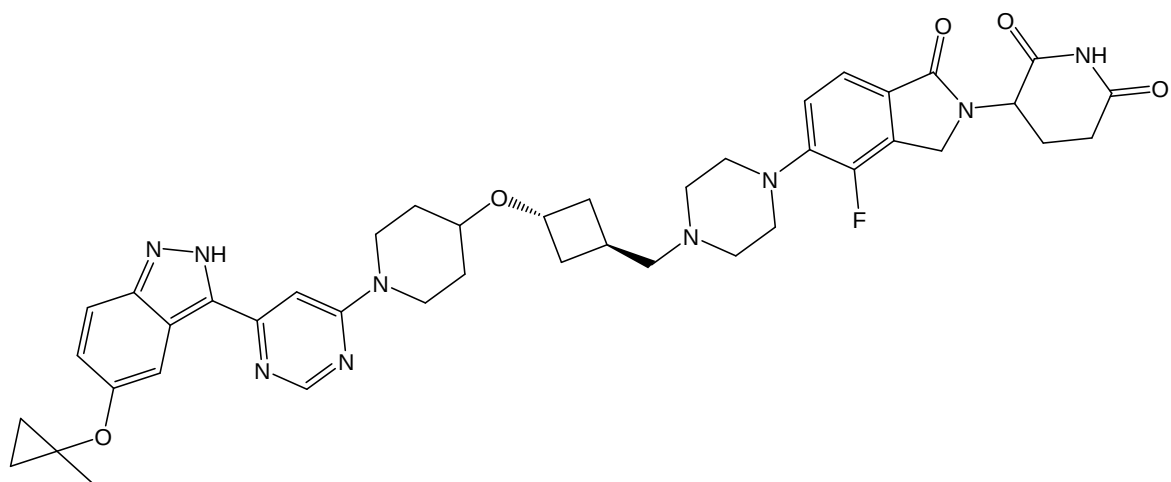


[illegible]C1CC2(C1)CCN(C2)CCN3CCCCC3c4ncnc5c4nc6ccc(OC7C8C(C7)C8)c6n5C1CC1Oc2ccc3c(c2)c4n[nH]4-c5ncnc5N6CCOC7CCCCC7C8CCN(C8)C9c1ccc2c(=O)[nH]c(=O)cc2c1F9

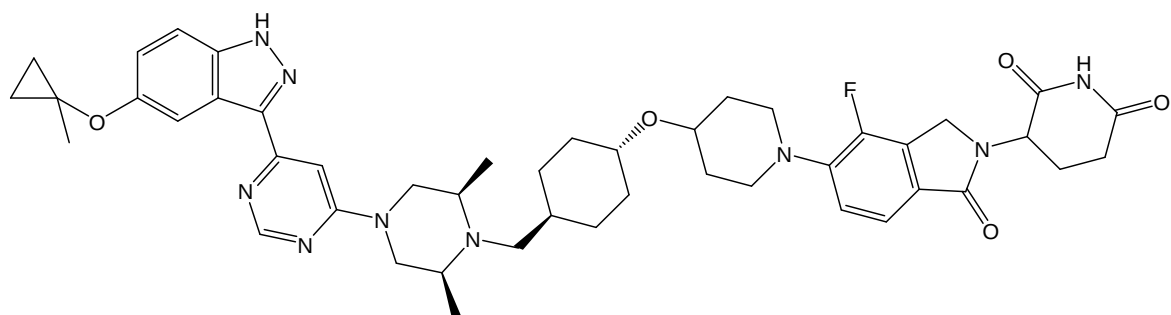
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CC1(C)OC2=CC=C3C(=C2)N=CN3C4=NC=CC5=N4CN(C5)N[C@H]6C[C@@H](C)[C@H](C7C[C@H](C8CCN(C8)COC9C=CC=C10C(=O)NC(=O)CC9=O)C=C(F)C10)C6COc1ccc2c(c1)c(=O)n(c2c3ccc(OC4CC4)c3)c5ccc(OC6CCN(C6)c7cc8nnc8cc(F)c7OC9CC9)cc5CC1(C)OC2=CC=C3C2=NC(=C3)C4=NC=CC(=N4)N5CCN(CC5)CCN6CCN(C6)C7C(F)(F)C8CCN8C9=C(F)C=C(C=C9)C(=O)N10C(=O)CC(=O)N10

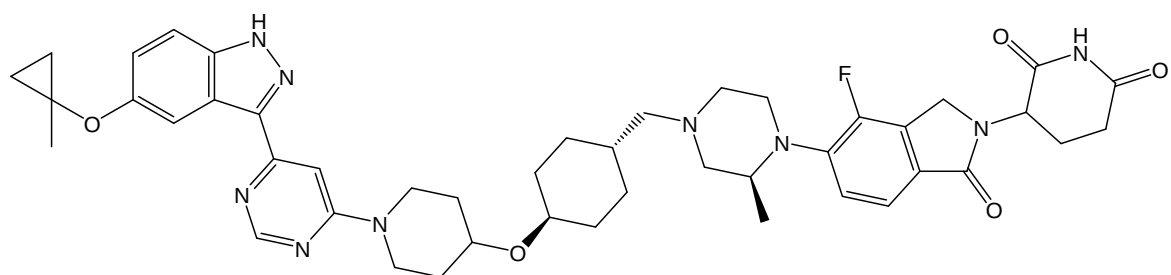
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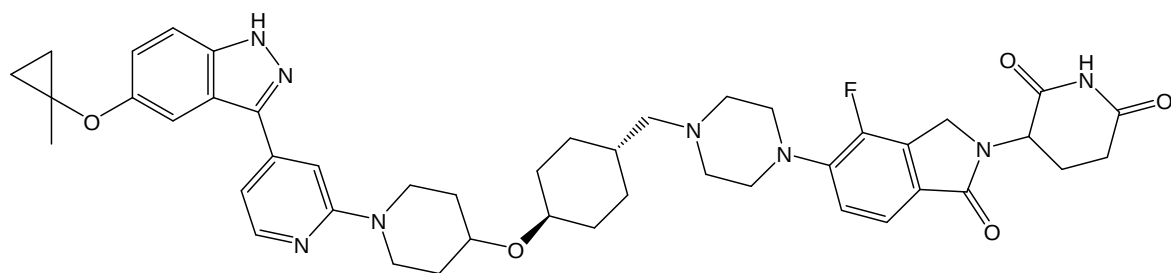
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(352),



(353),



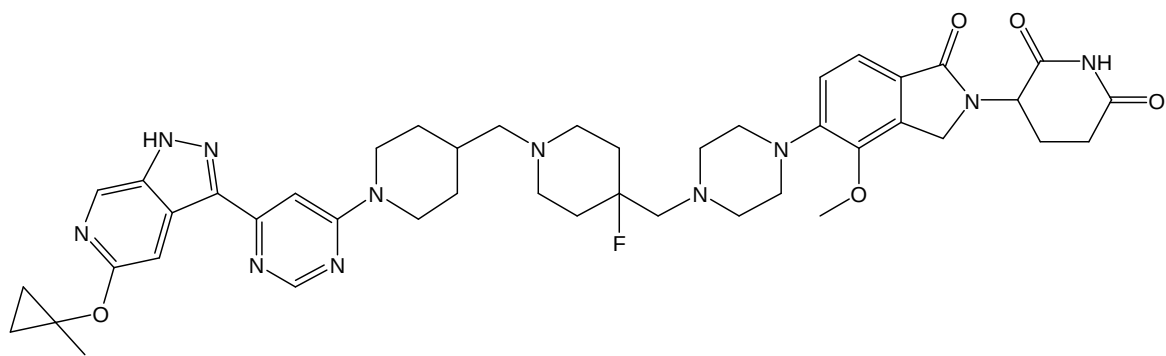
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COC1=CC=C2C(=C1)C(=O)N(C2)C3=CC=CC=C3C4CCN(C4)CC5CCN(C5)C6OC6C7CCN(C7)C8=CN=C(N9C=CC=C(C=C9)CO10C1CC1)C8=NCC1(C)OC1c2ccc3c(c2)c4nnc3c4c5ncnc5N6CCCCC6OCCN7CC8(C(F)(F)C8)CCN7c9cc(OC)c10c(c9)c(=O)n(c10)C(=O)N11CCCC(=O)N11C1CC1Oc2ccc3c(c2)c4n[nH]4-c5ccc6c(c5)nc7c6c8c(c7)nc(=O)c9ccccc89-c10ccn10-c11ccccc11

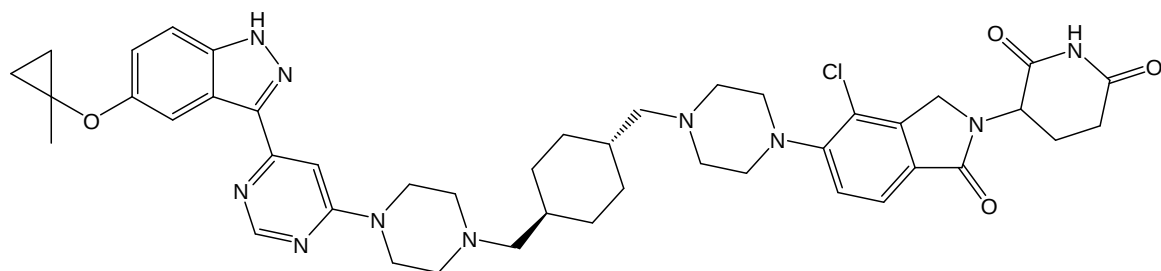
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COC1=CC=C2C(=O)N(C1)c3ccccc3CO[C@H]4CCCC[C@@H]4CN5CCN(CC5)c6nc7c(ncn7C8=CC=C(F)C(OC9CC9)=C8)C2=OCC1(C)OC2=CC=C(C=C2C3=NN=C4C(=C3)N=CN=C4N5CCN(CCC6C=CC(=C6)C(=O)NC7C(=O)CCNC7=O)C6)CCN5C8CCCCC8O[C@H]9CCCC[C@@H]9CN1(C)CCC1(C)OC1c2ccc3c(c2)c4nnc3c4c5ncnc5N6CCCCC6OCCN7C8CCCC8(C(F)(F)F)CC7c9cc10c(cc9)c(=O)n(c10)c11c(=O)[nH]c11=O

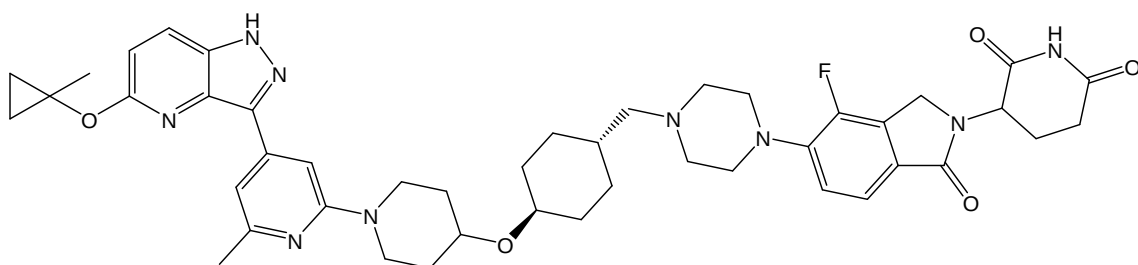
COC1=CC=C2C(=C1)N(C(=O)NC(=O)CCC2=O)C3=CC=C(N3CN(C)C)C[C@H]4CCCC[C@@H]4CO[N+]56CCN(CC5)CCN6C7=NN=C8C9=CC=C(C=C8)C(=C9)C10=CC=CC=C10OCC12CCCCC12CC1(C)OC2=CC=C(C=C2C3=NN=C(C3=N4C=NC(=N4)N5C6C(C(C6)C7C(C(C7)C8C(C(C8)C9C(=O)NC(=O)CC9=O)C(=O)O)C=C(C=C5C=C(C=C5)OC)N1C)C)C)CCC1(C)OC1c2ccc3nc(C4=CN=CN4C5CCN(CC5)OC6CCCCC6OC7CCCCN7c8cc(F)ccc9c8c(=O)nc(=O)CC9=O)nc3c2



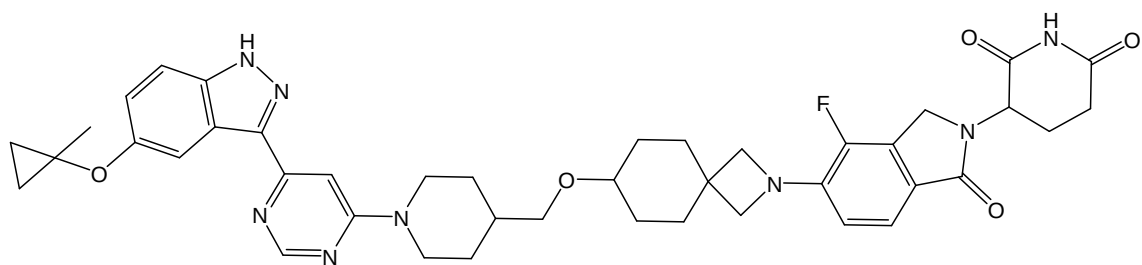
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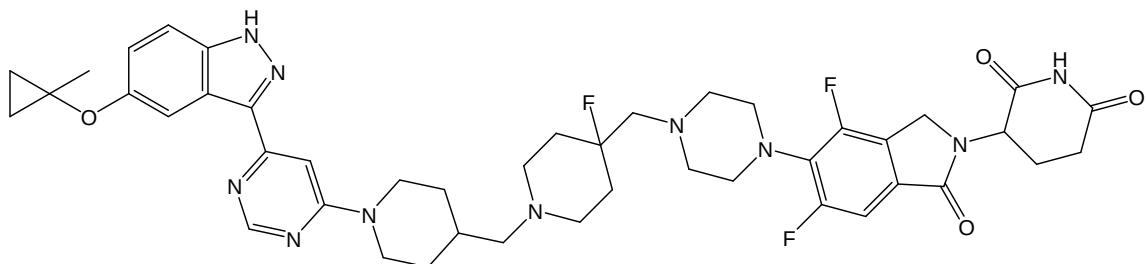
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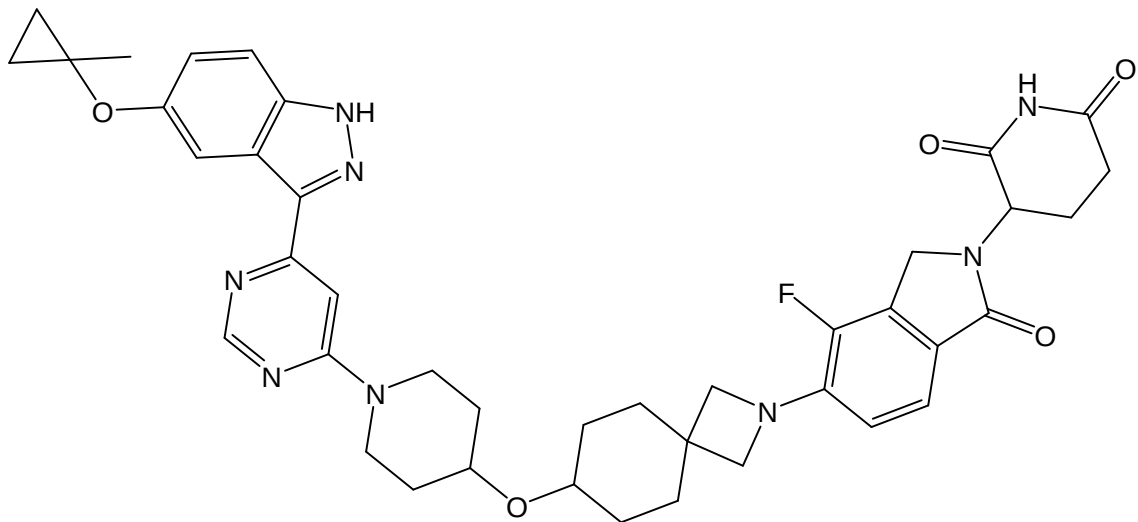
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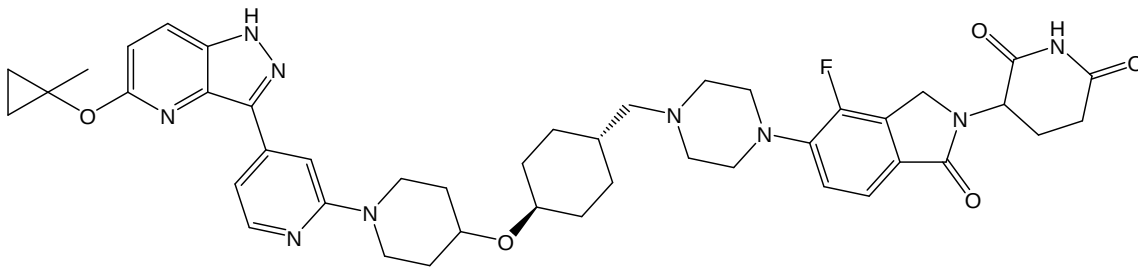
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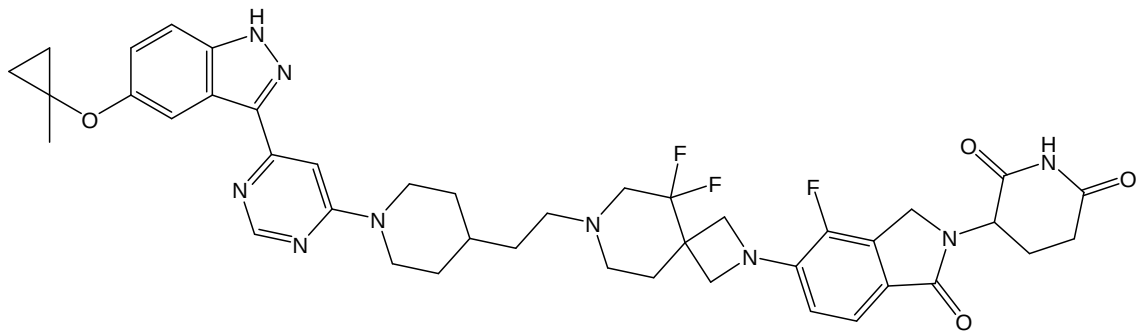
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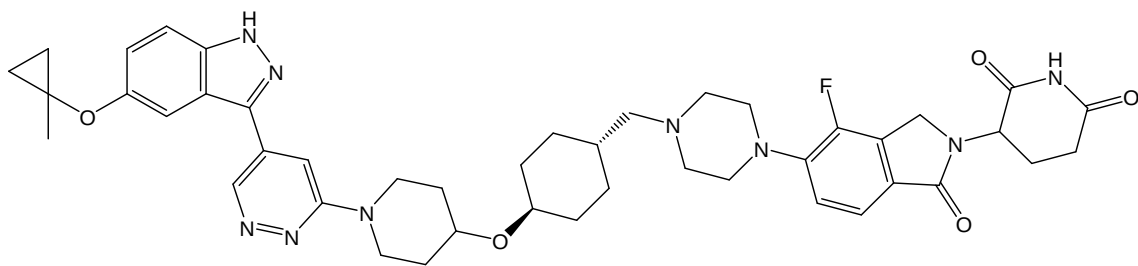
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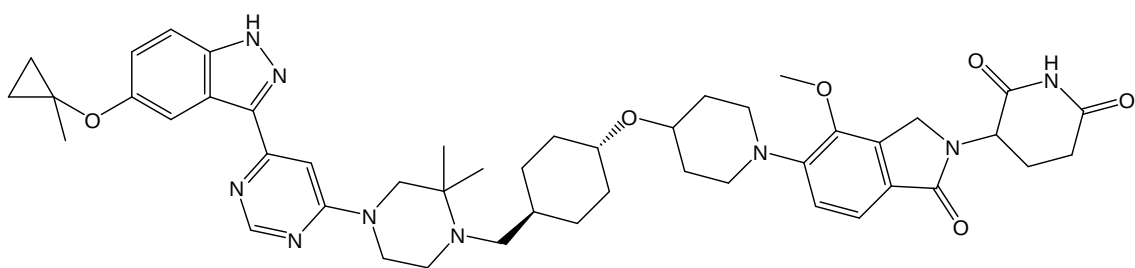
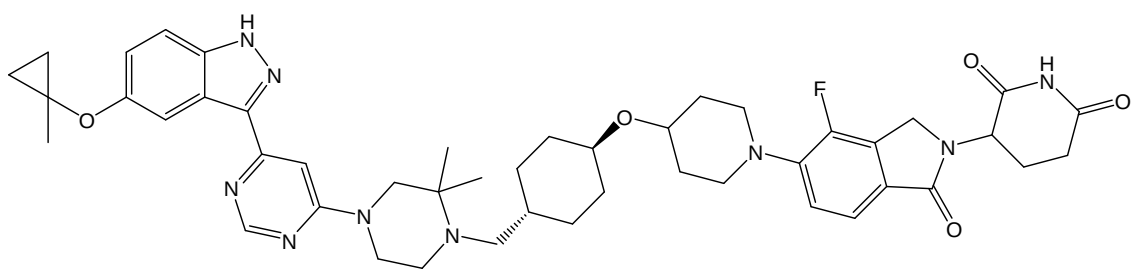
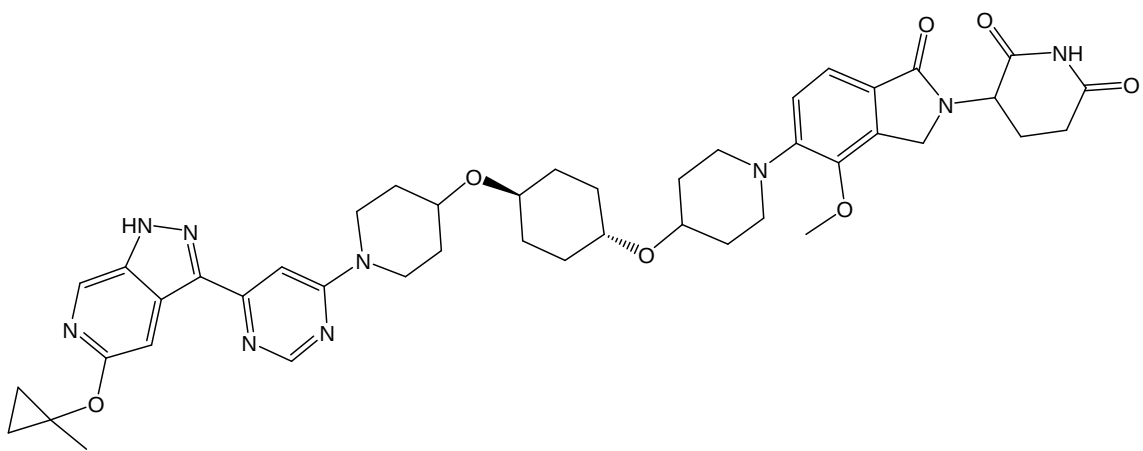
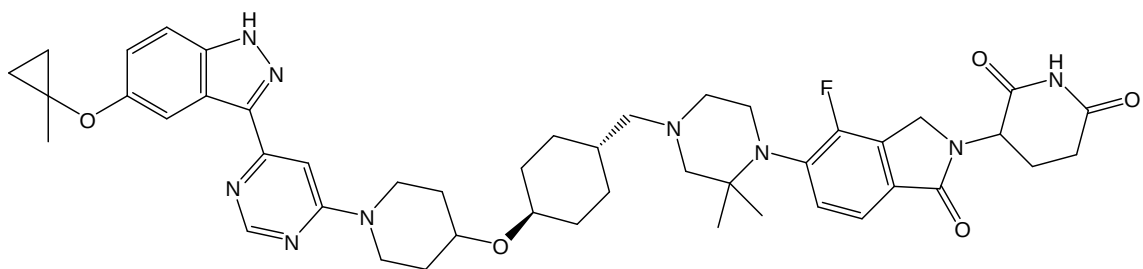
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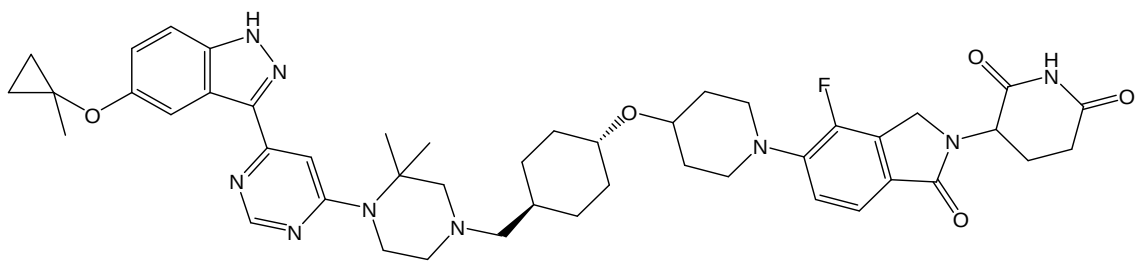


(376),

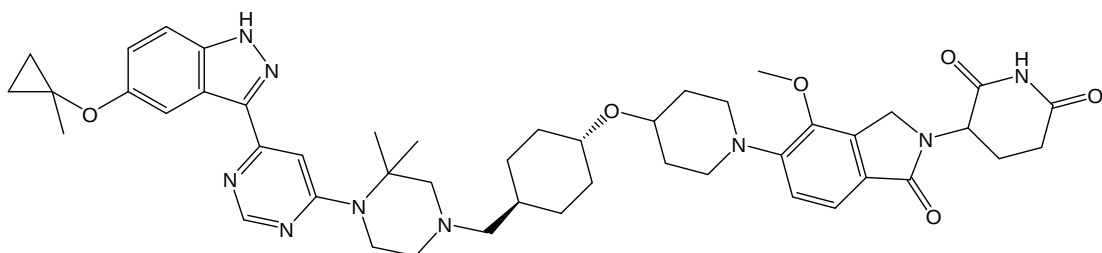


(377),



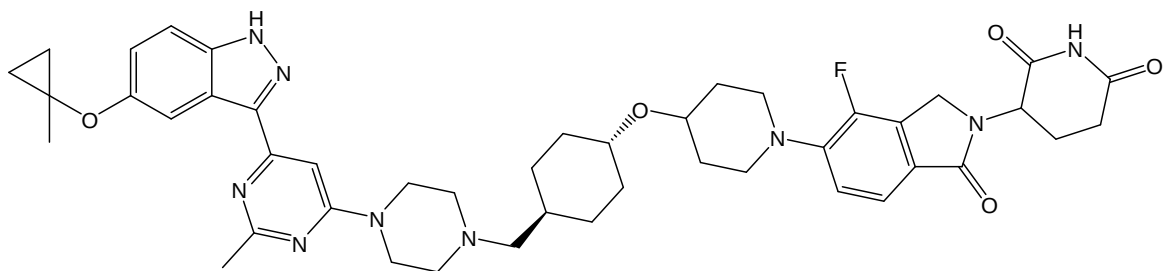


(383) y

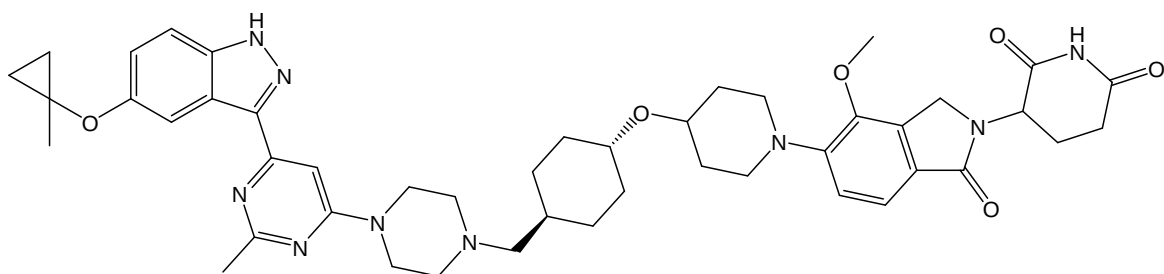


(384), o enantiómeros de esta.

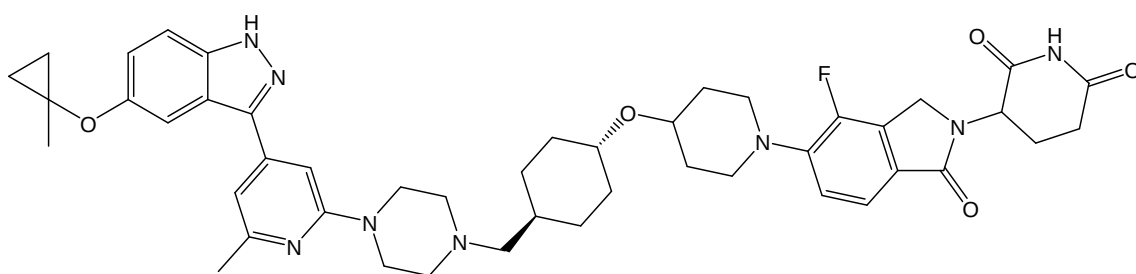
43. Un compuesto que se selecciona de:



(365),



(367) y



(379), o enantiómeros de esta.

44. Una composición que comprende una cantidad eficaz de un compuesto bifuncional de cualquiera de las reivindicaciones 1-43 y un portador farmacéuticamente aceptable.
45. La composición de la reivindicación 44, en donde la composición comprende, además, un agente bioactivo adicional.
46. La composición de la reivindicación 45, en donde el agente bioactivo adicional es un antiinflamatorio, un agente quimioterapéutico o un agente inmunomodulador.
47. Una composición que comprende un portador farmacéuticamente aceptable y una cantidad eficaz de al menos un compuesto de cualquiera de las reivindicaciones 1-43 para tratar una enfermedad, un trastorno o un síntoma relacionado causalmente con LRRK2 en un sujeto, en donde la composición es eficaz para tratar o mejorar la enfermedad, trastorno o al menos un síntoma de la enfermedad o trastorno.
48. La composición de la reivindicación 47, en donde la enfermedad o trastorno es enfermedad de Parkinson (PD) idiopática, PD asociada a la mutación de LRRK2, tauopatías primarias, demencia de cuerpos de Lewy, enfermedad de Crohn, lepra, neuroinflamación, parálisis supranuclear progresiva, enfermedad de Picks, FTDtau, demencia temporal frontal TDP-43, ALS TDP-43, ALS c9orf, enfermedad de Huntington, ataxias espinocerebelosas (SCA) 1, 2, 3, 6, 7 y 17, atrofia palidolusiana dentatorubral (DRPLA) o enfermedad de Kennedy.
49. Un método para tratar o prevenir una enfermedad, un trastorno o síntoma asociado con LRRK2 que comprende, proporcionar a un paciente que lo necesite y administrarle una cantidad eficaz de un compuesto como se describe en la presente o composición que lo comprende al paciente, en donde el compuesto o composición es eficaz para tratar o mejorar la enfermedad, trastorno o al menos un síntoma de la enfermedad o trastorno.