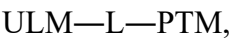


REIVINDICACIONES

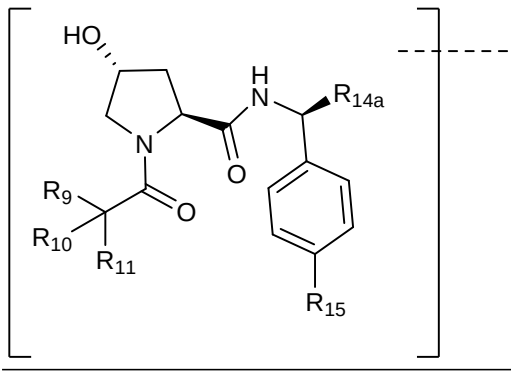
1. Un compuesto que tiene la estructura química:



o una de sus sales aceptables farmacéuticamente,

en donde:

la ULM está representada por la estructura:

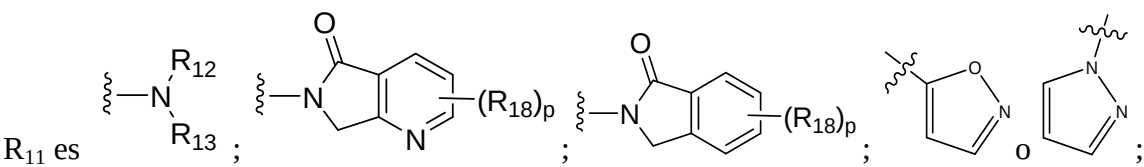


en donde:

es H, C₁₋₆ alquilo, C₁₋₆ haloalquilo, C₁₋₆ alquilo-OH, o ciclopropilo;

R₉ es H;

R₁₀ es H, etilo, isopropilo, tert-butilo, sec-butilo, ciclopropilo, ciclobutilo, ciclopentilo, o ciclohexilo;



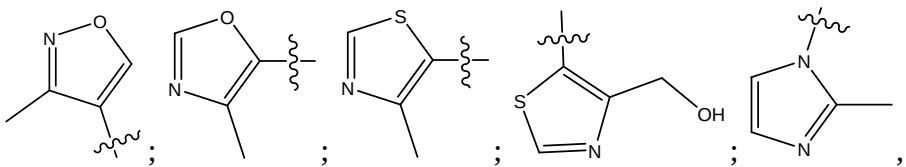
p es 0, 1, 2, 3, o 4;

cada R₁₈ es independientemente halo, alcoxi, ciano, alquilo, haloalquilo, haloalcoxi;

R₁₂ es H, C=O;

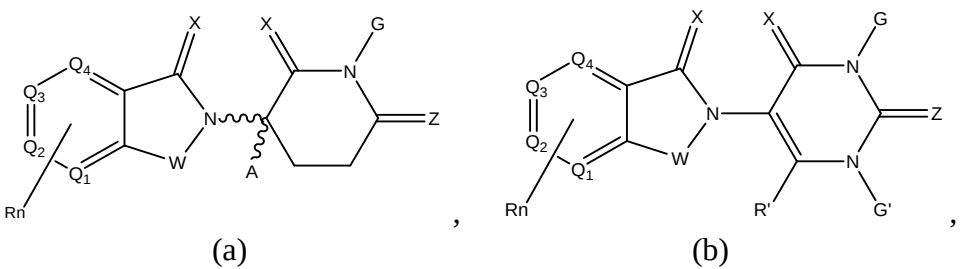
R₁₃ es H, C₁₋₆ alquilo, o C₁₋₆ alquilcarbonilo; y

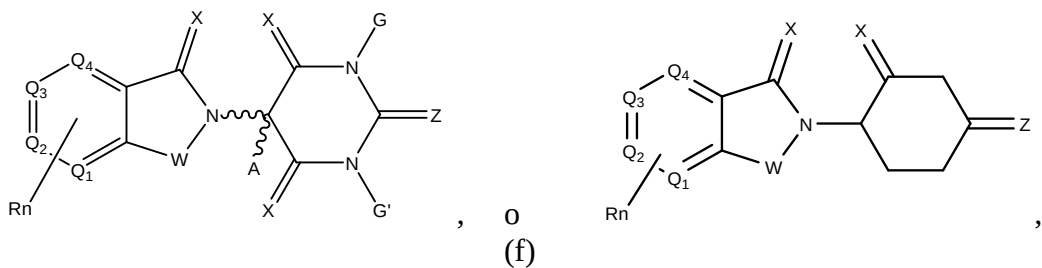
R₁₅ se selecciona de H, halo, CN, OH, y NO₂;



en donde la línea discontinua indica el punto de acoplamiento de una porción de enlazador químico;

o en donde la ULM está representada por la estructura:

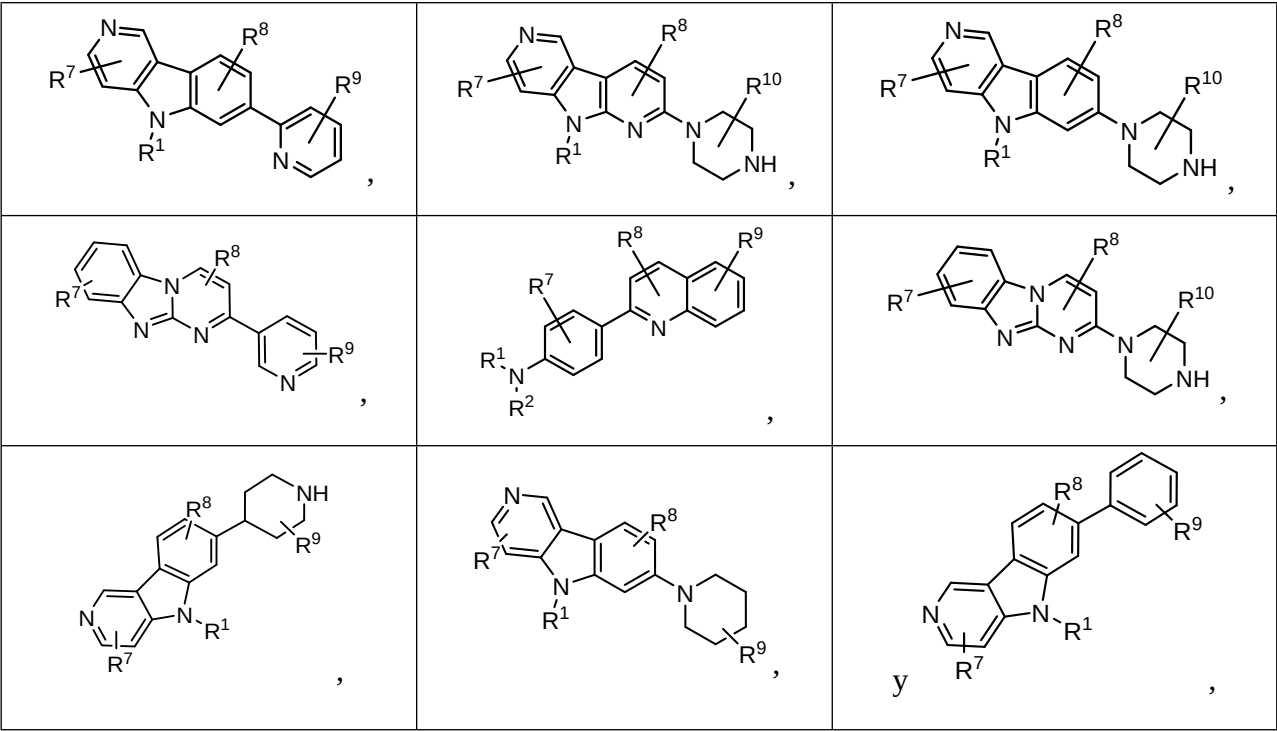




en donde:

- W es CH₂ o C=O;
- cada X se selecciona independientemente de O, S, y H₂;
- Z se selecciona de O, S, y H₂;
- G y G' se seleccionan independientemente cada una de H, C₁₋₆ alquilo, OH, y bencilo
opcionalmente sustituido con R' ;
- Q₁, Q₂, Q₃, y Q₄ representan un carbono sustituido con un grupo independientemente
seleccionado de R' , N o N-óxido;
- A se selecciona independientemente de H, Cl, y F;
- R comprende -CONR'R'', -OR', -NR'R'', -SR', -SO₂R', -SO₂NR'R'', -CR'R''-, -CR'NR'R''-,
-P(O)(OR')R'', -P(O)R'R'', -OP(O)(OR')R'', -OP(O)R'R'', -Cl, -F, -Br, -I, -CF₃, -CN, -
NR'SO₂NR'R'', -NR'CONR'R'', -CONR'COR'', -NR'C(=N-CN)NR'R'', -C(=N-
CN)NR'R'', -NR'C(=N-CN)R'', -NR'C(=C-NO₂)NR'R'', -SO₂NR'COR'', -NO₂, -CO₂R',
-C(C=N-OR')R'', -CR'=CR'R'', -CCR', -S(C=O)(C=N-R')R'', -SF₅, o -OCF₃;
- R' y R'' se seleccionan independientemente de un enlace, H, N, N-óxido, o -C(=O)R;
- ~~~~ representa un enlace que puede ser estereoespecífico o no estereoespecífico; y
- en donde n es 1, 2, 3, or4, y en donde
- cuando n es 1, R_n está modificada para estar unida covalentemente al grupo enlazador (L), y
- cuando n es 2, 3, o 4, entonces un R_n está modificada para estar unida covalentemente al grupo
enlazador (L);

la PTM se representa mediante una estructura química seleccionada de:



en donde:

la PTM esta modificada para estar covalentemente unida a L;

R¹ y R² se seleccionan independientemente de H, C₁₋₆alquilo opcionalmente sustituido 1-3 veces con halo; y

R⁷, R⁸, R⁹ y R¹⁰ son 1 a 4 sustituyentes independientemente seleccionados de H, C₁₋₆alquilo, C₁₋₆haloalquilo, halo, hidroxilo, amino, acetilamino, o ciano;

o dos grupos R9 tomados juntos con el átomo al que se unen para, formar heterociclilo de 3-11 miembros; y

el L está representado por la fórmula:



en donde:

A es un grupo que se conecta a la porción ULM o PTM; y

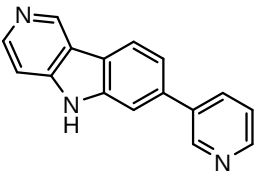
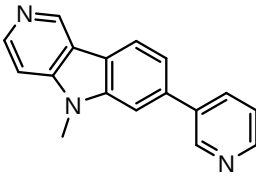
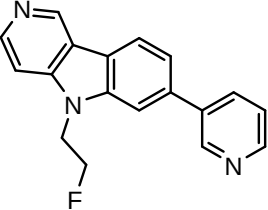
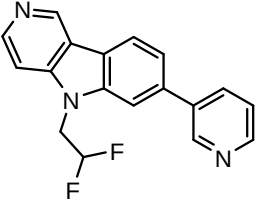
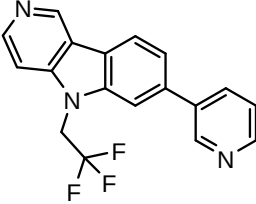
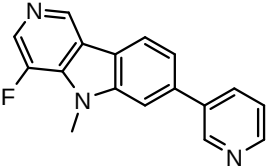
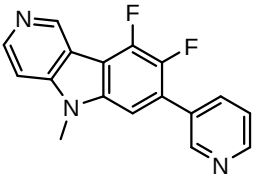
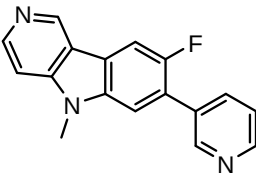
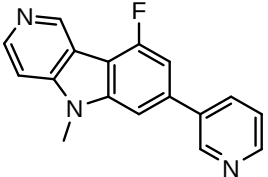
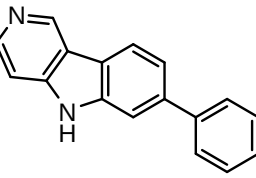
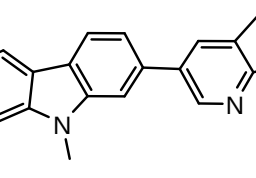
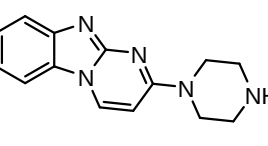
q es 1-50,

en donde A se selecciona de un enlace, CR^{L1}R^{L2}, O, S, SO, SO₂, NR^{L3}, CO, CR^{L1}=CR^{L2}, C≡C, cicloalquilo de C₃₋₁₁ opcionalmente sustituido con 1 o 2 grupos R^{L1} y/o R^{L2}, heterociclilo de 3-11 miembros opcionalmente sustituido con 1 o 2 grupos R^{L1} y/o R^{L2}, C₆₋₁₀ arilo opcionalmente sustituido con 1 o 2 grupos R^{L1} y/o R^{L2}, heteroarilo de 6-10 miembros opcionalmente sustituido con 1 o 2 grupos R^{L1} y/o R^{L2}, donde R^{L1} o R^{L2}, cada uno independientemente se unen opcionalmente a otros grupos para formar C₃₋₁₁ cicloalquilo y/o heterociclilo de 3-11 miembros opcionalmente sustituidos con 1 o 2 grupos R^{L5};

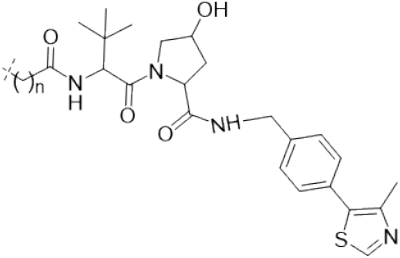
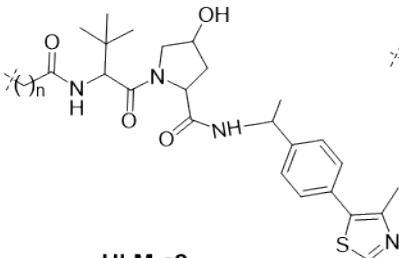
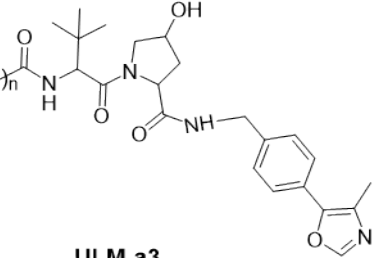
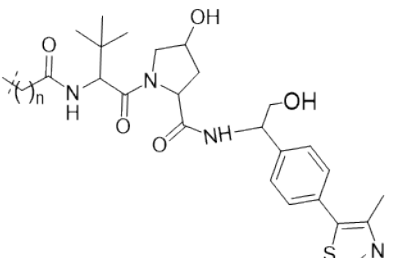
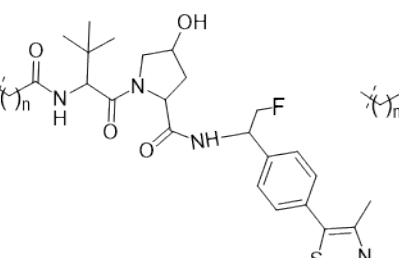
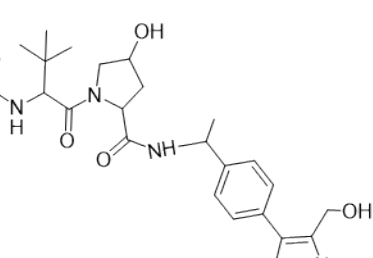
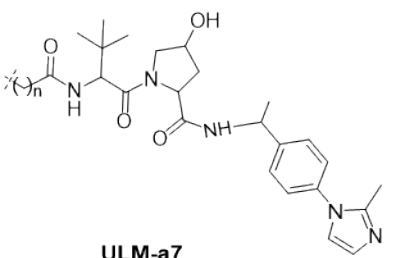
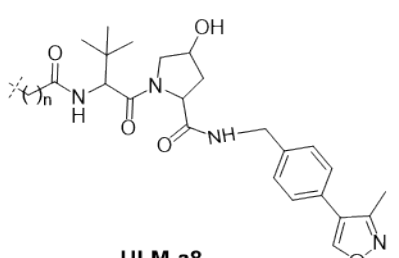
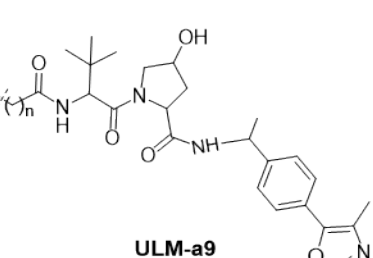
R^{L1}, R^{L2}, R^{L3}, R^{L4} y R^{L5} son, cada uno independientemente, seleccionados de halo, alquilo de C₁₋₈, OC₁₋₈alquilo, SC₁₋₈alquilo, NHC₁₋₈alquilo, N(C₁₋₈alquilo)₂, C₃₋₁₁cicloalquilo, heterociclilo de 3-11 miembros, OC₁₋₈cicloalquilo, SC₁₋₈cicloalquilo, NHC₁₋₈cicloalquilo, N(C₁₋₈cicloalquilo)₂, N(C₁₋₈cicloalquilo)(C₁₋₈alquilo), OH, NH₂, CC-C₁₋₈alquilo, CCH, CH=CH(C₁₋₈alquilo), C(C₁₋₈alquilo)=CH(C₁₋₈alquilo), C(C₁₋₈alquilo)=C(C₁₋₈alquilo)₂, COC₁₋₈alquilo, CO₂H, CN, CF₃, CHF₂, CH₂F, NO₂, 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₋

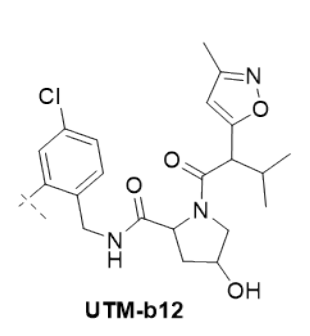
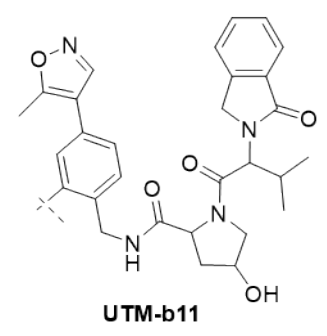
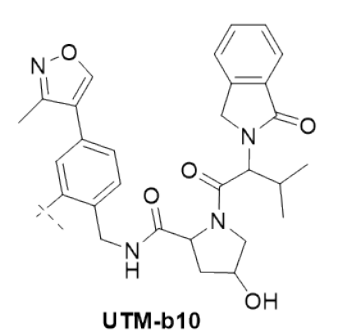
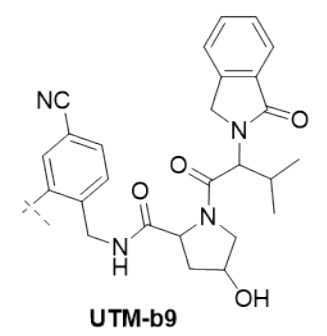
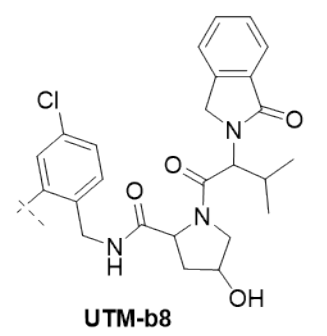
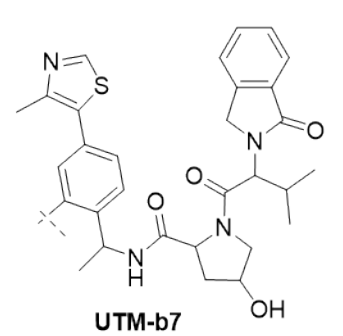
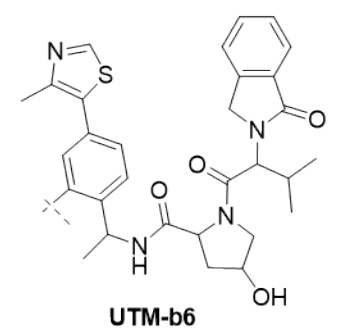
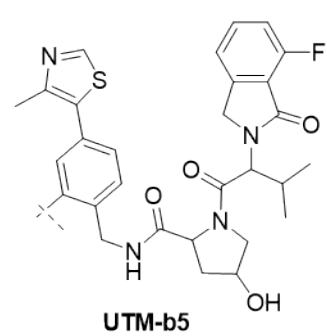
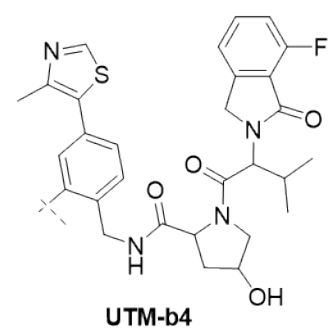
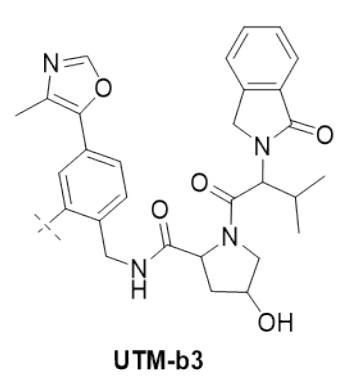
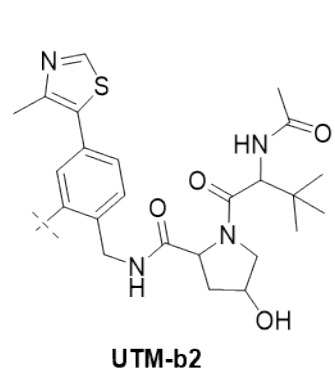
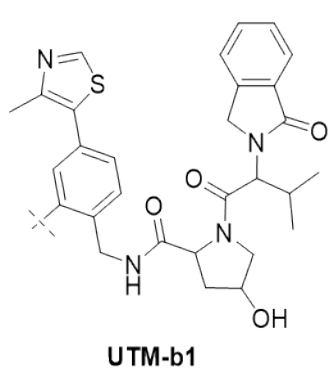
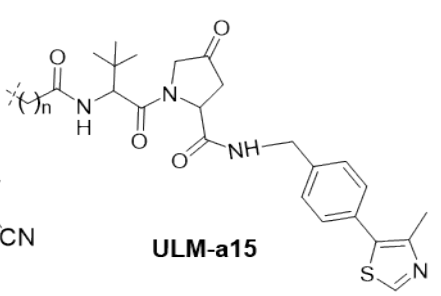
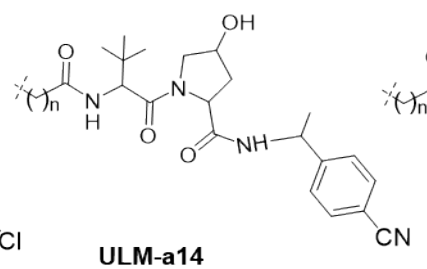
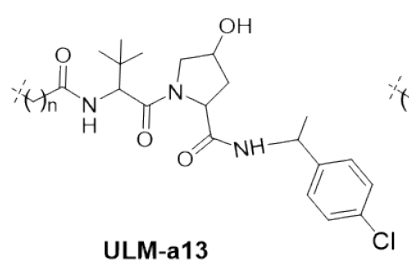
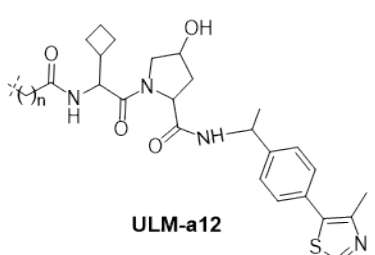
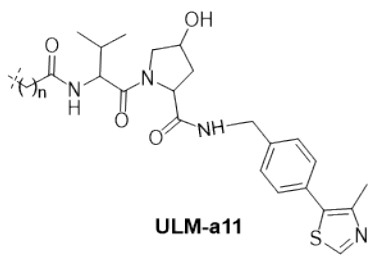
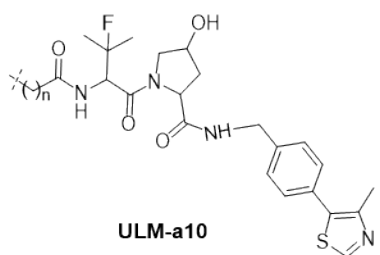
8alquilo)SO₂NH(C₁₋₈alquilo), N(C₁₋₈alquilo) SO₂N(C₁₋₈alquilo)₂, NH SO₂NH(C₁₋₈alquilo), NH SO₂N(C₁₋₈alquilo)₂, y NH SO₂NH₂.

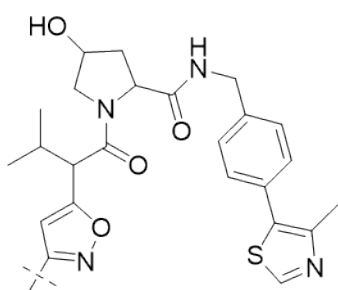
2. El compuesto de conformidad con la reivindicación 1, en donde la PTM se representa mediante una estructura química seleccionada de:

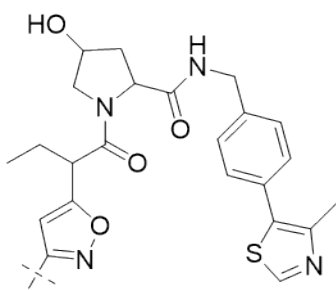
3. El compuesto de conformidad con la reivindicación 1 o reivindicación 2, en donde la ULM comprende un grupo seleccionado de:

		
ULM-a1	ULM-a2	ULM-a3
		
ULM-a4	ULM-a5	ULM-a6
		
ULM-a7	ULM-a8	ULM-a9

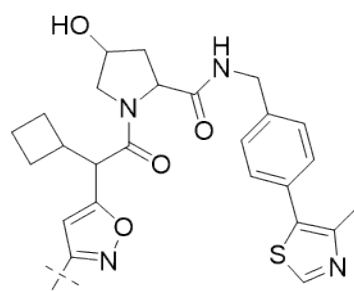




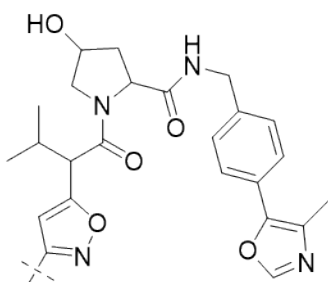
UTM-c1



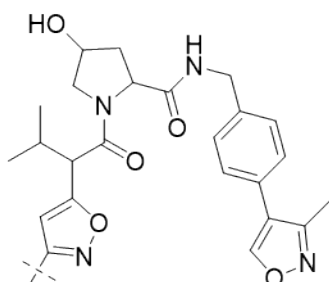
UTM-c2



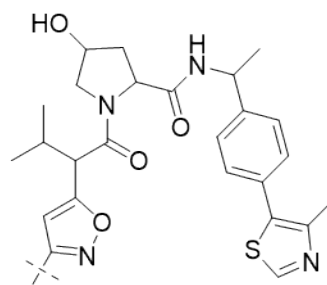
UTM-c3



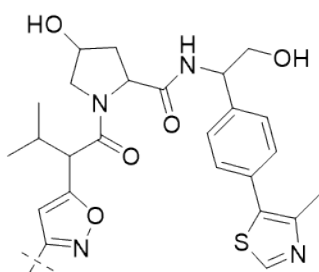
UTM-c4



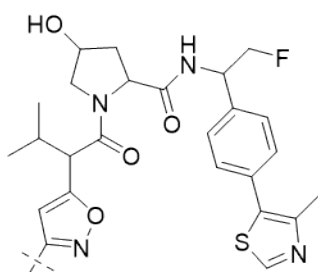
UTM-c5



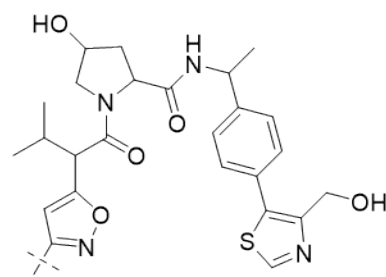
UTM-c6



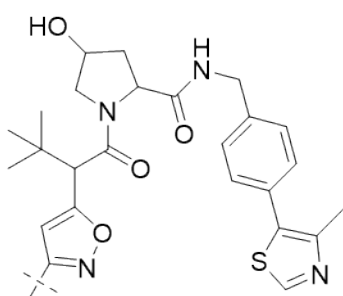
UTM-c7



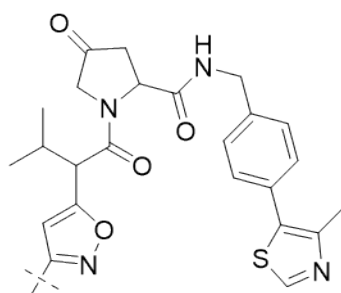
UTM-c8



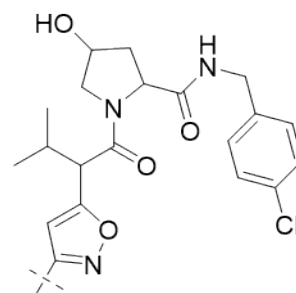
UTM-c9



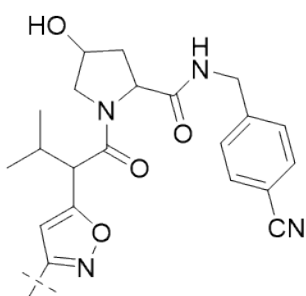
UTM-c10



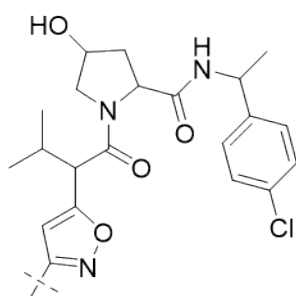
UTM-c11



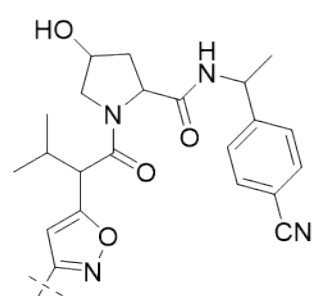
UTM-c12



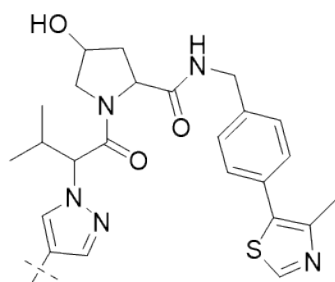
UTM-c13



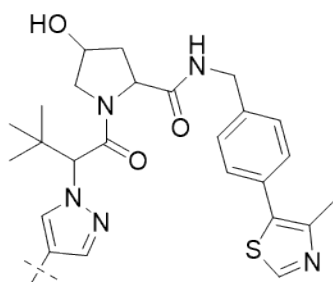
UTM-c14



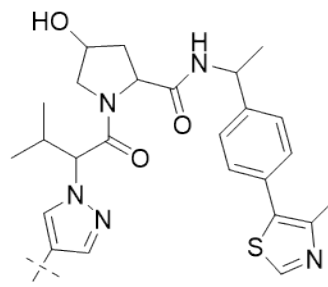
UTM-c15



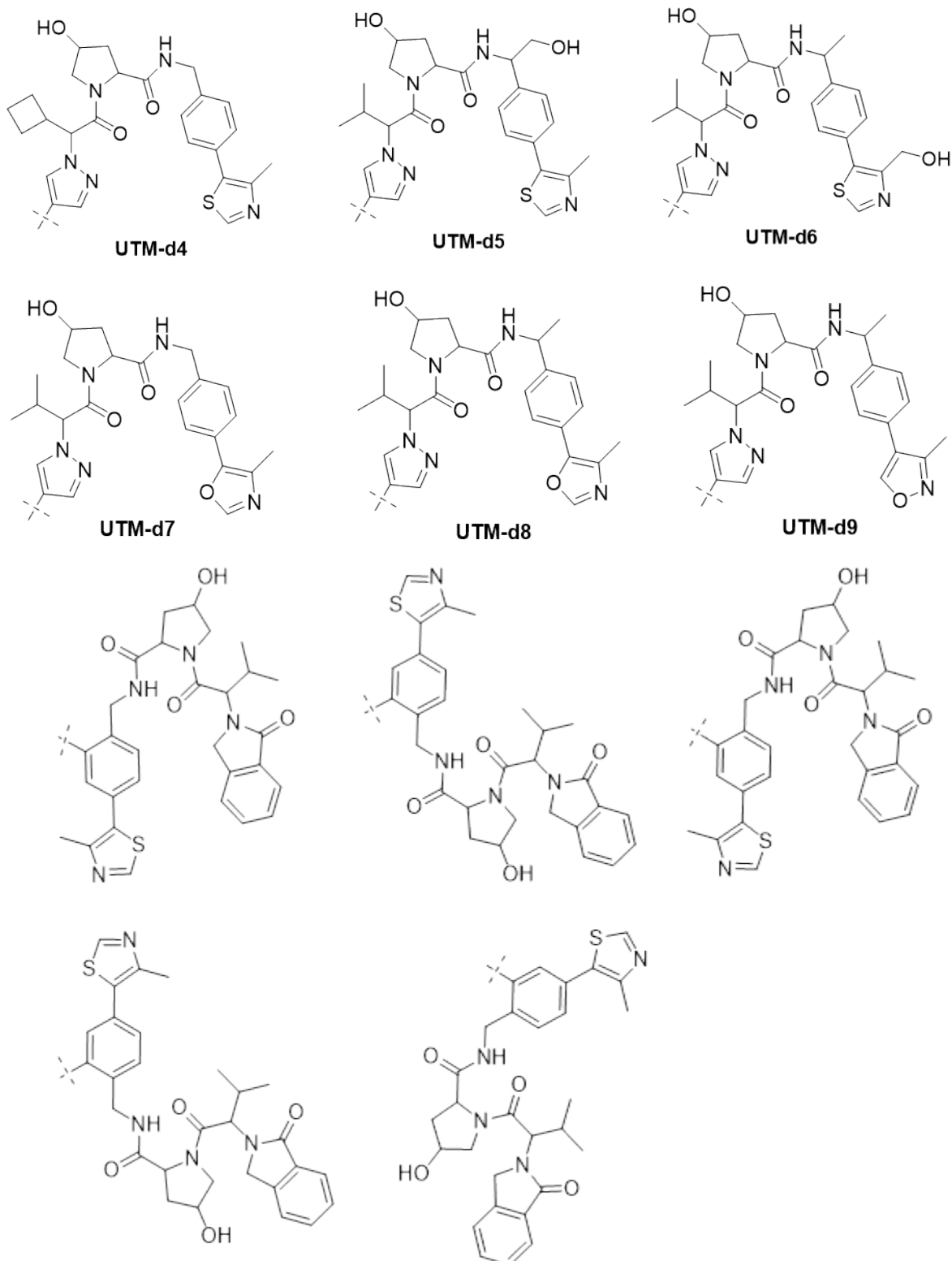
UTM-d1



UTM-d2

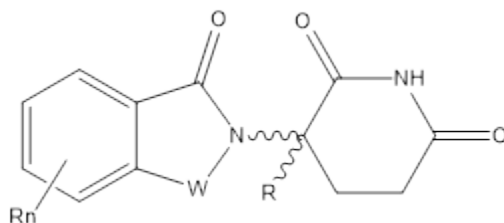


UTM-d3



en donde el anillo fenilo en la ULM-a1 hasta la ULM -a15, ULM -b1 hasta la ULM-b12, ULM-c1 hasta la ULM-c15 y ULM-d1 hasta la ULM-d9 se sustituye opcionalmente con fluor, y en donde la línea discontinua indica el punto de acoplamiento de la porción de enlazador químico.

4. El compuesto de conformidad con la reivindicación 1 o reivindicación 2, en donde la CLM tiene una estructura química representada por:



en donde:

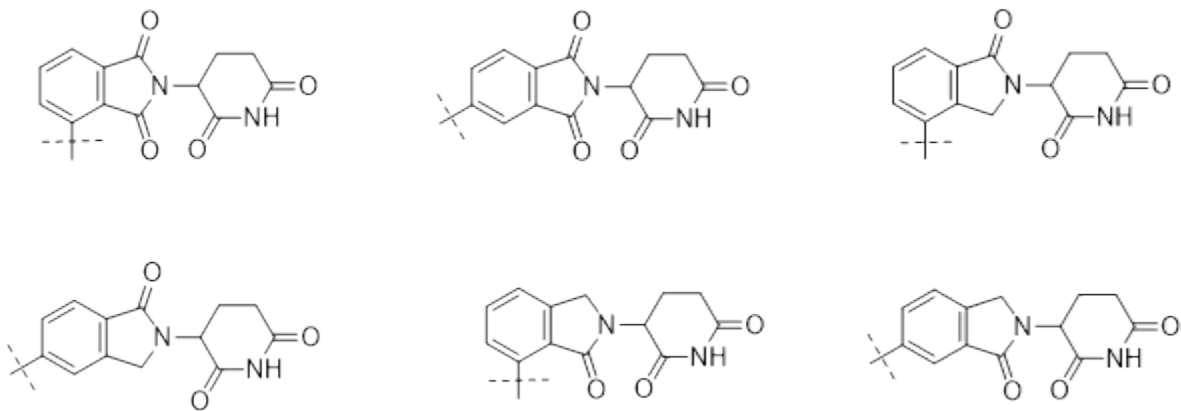
W se selecciona independientemente del grupo CH_2 , $C=O$, y NH ;

R se selecciona independientemente de un H o C₁₋₆ alquilo;

~~~~ representa un enlace que puede ser estereoespecífico o no estereoespecífico; y

R<sub>n</sub> comprende un grupo enlazador químico (L), que está modificado para estar covalentemente unido a la PTM.

5. El compuesto de conformidad con alguna de las reivindicaciones 1, 2, o 4, en donde la CLM tiene una estructura química representada por:



en donde las líneas discontinuas indican los puntos de acoplamiento del enlazador.

6. El compuesto de conformidad con alguna de las reivindicaciones 1 a 5, en donde el enlazador (L) comprende un grupo representado por una estructura general seleccionada de:

-N(R)-(CH<sub>2</sub>)<sub>m</sub>-O(CH<sub>2</sub>)<sub>n</sub>-O(CH<sub>2</sub>)<sub>o</sub>-O(CH<sub>2</sub>)<sub>p</sub>-O(CH<sub>2</sub>)<sub>q</sub>-O(CH<sub>2</sub>)<sub>r</sub>-OCH<sub>2</sub>-,

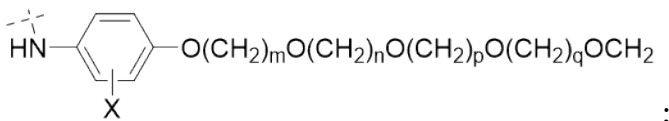
-O-(CH<sub>2</sub>)<sub>m</sub>-O(CH<sub>2</sub>)<sub>n</sub>-O(CH<sub>2</sub>)<sub>o</sub>-O(CH<sub>2</sub>)<sub>p</sub>-O(CH<sub>2</sub>)<sub>q</sub>-O(CH<sub>2</sub>)<sub>r</sub>-OCH<sub>2</sub>-,

-O-(CH<sub>2</sub>)<sub>m</sub>-O(CH<sub>2</sub>)<sub>n</sub>-O(CH<sub>2</sub>)<sub>o</sub>-O(CH<sub>2</sub>)<sub>p</sub>-O(CH<sub>2</sub>)<sub>q</sub>-O(CH<sub>2</sub>)<sub>r</sub>-O-;

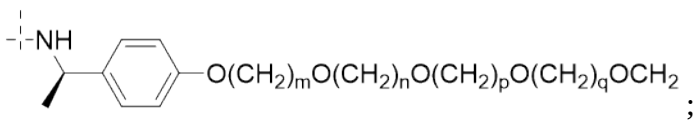
-N(R)-(CH<sub>2</sub>)<sub>m</sub>-O(CH<sub>2</sub>)<sub>n</sub>-O(CH<sub>2</sub>)<sub>o</sub>-O(CH<sub>2</sub>)<sub>p</sub>-O(CH<sub>2</sub>)<sub>q</sub>-O(CH<sub>2</sub>)<sub>r</sub>-O-;

-(CH<sub>2</sub>)<sub>m</sub>-O(CH<sub>2</sub>)<sub>n</sub>-O(CH<sub>2</sub>)<sub>o</sub>-O(CH<sub>2</sub>)<sub>p</sub>-O(CH<sub>2</sub>)<sub>q</sub>-O(CH<sub>2</sub>)<sub>r</sub>-O-;

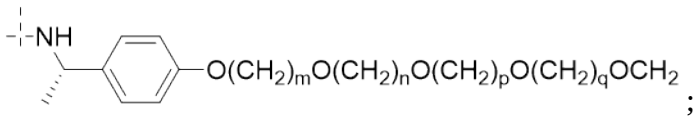
-(CH<sub>2</sub>)<sub>m</sub>-O(CH<sub>2</sub>)<sub>n</sub>-O(CH<sub>2</sub>)<sub>o</sub>-O(CH<sub>2</sub>)<sub>p</sub>-O(CH<sub>2</sub>)<sub>q</sub>-O(CH<sub>2</sub>)<sub>r</sub>-OCH<sub>2</sub>-;



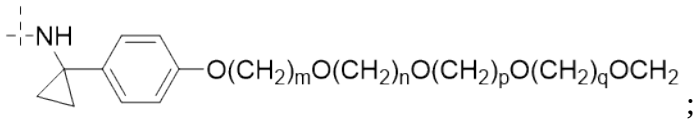
;



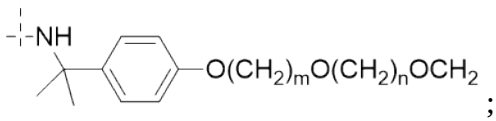
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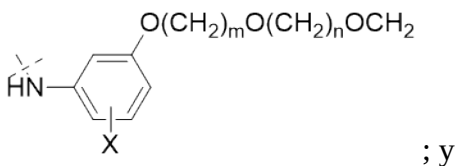
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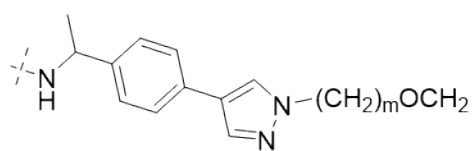
;



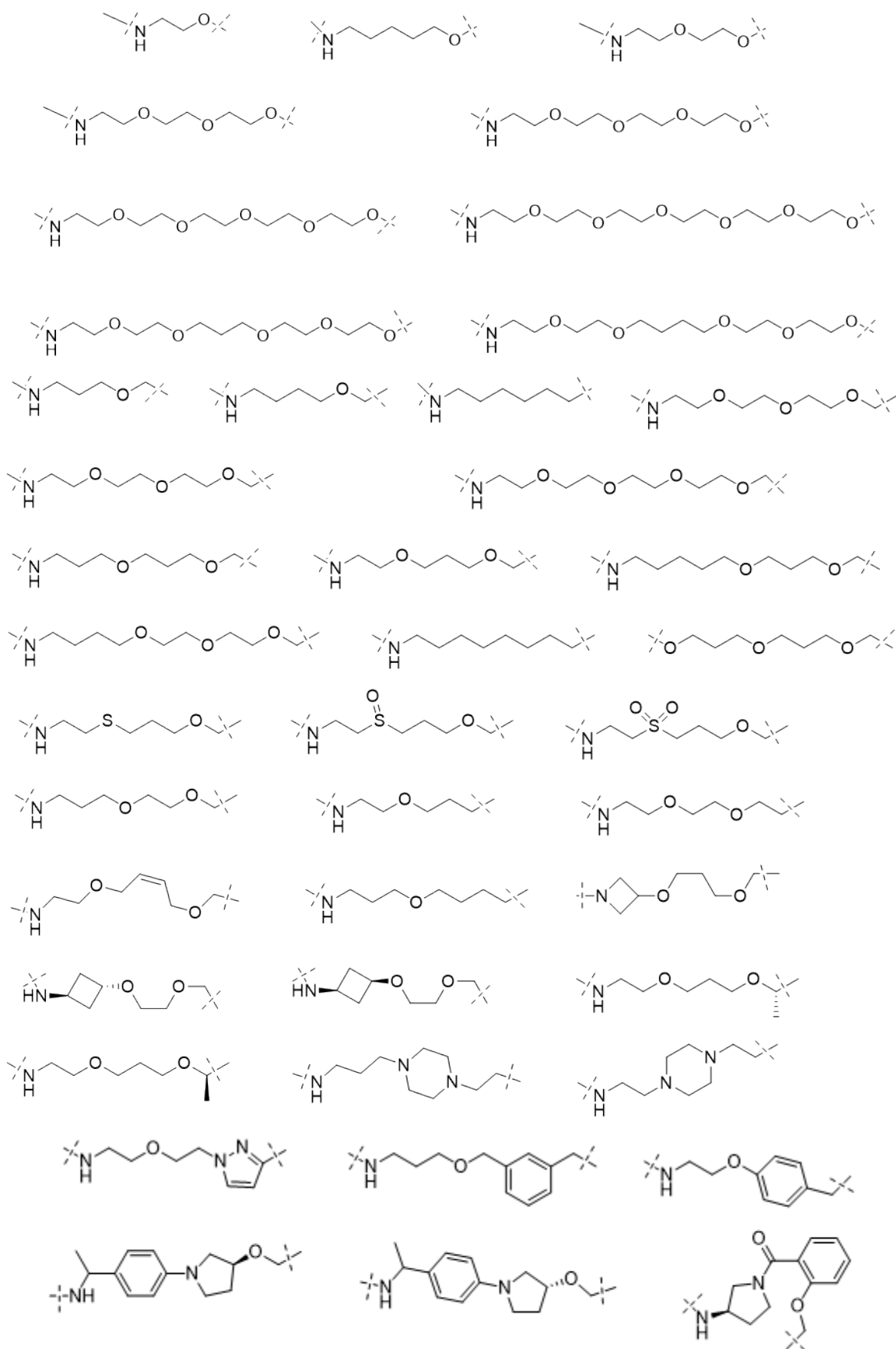
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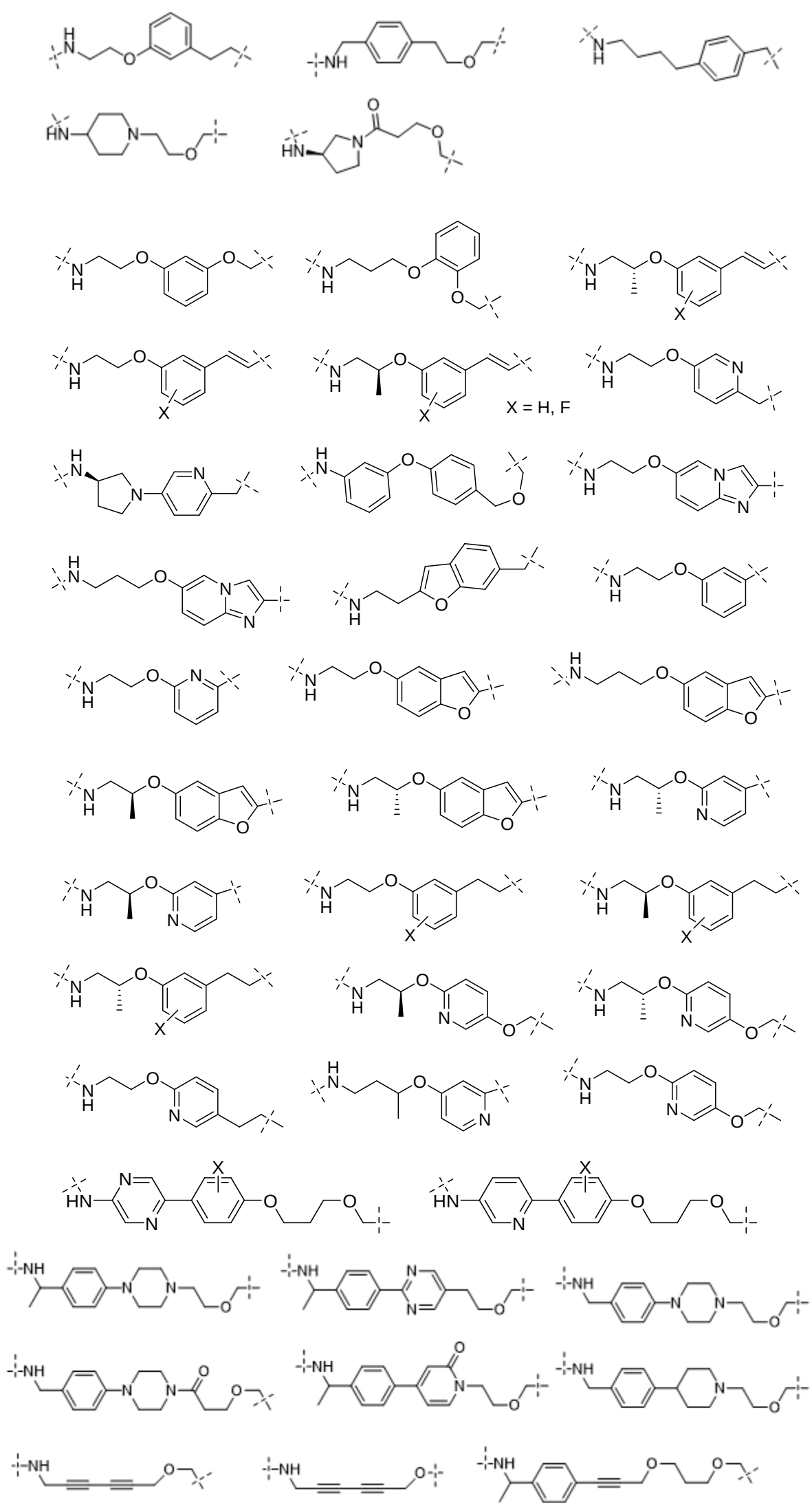


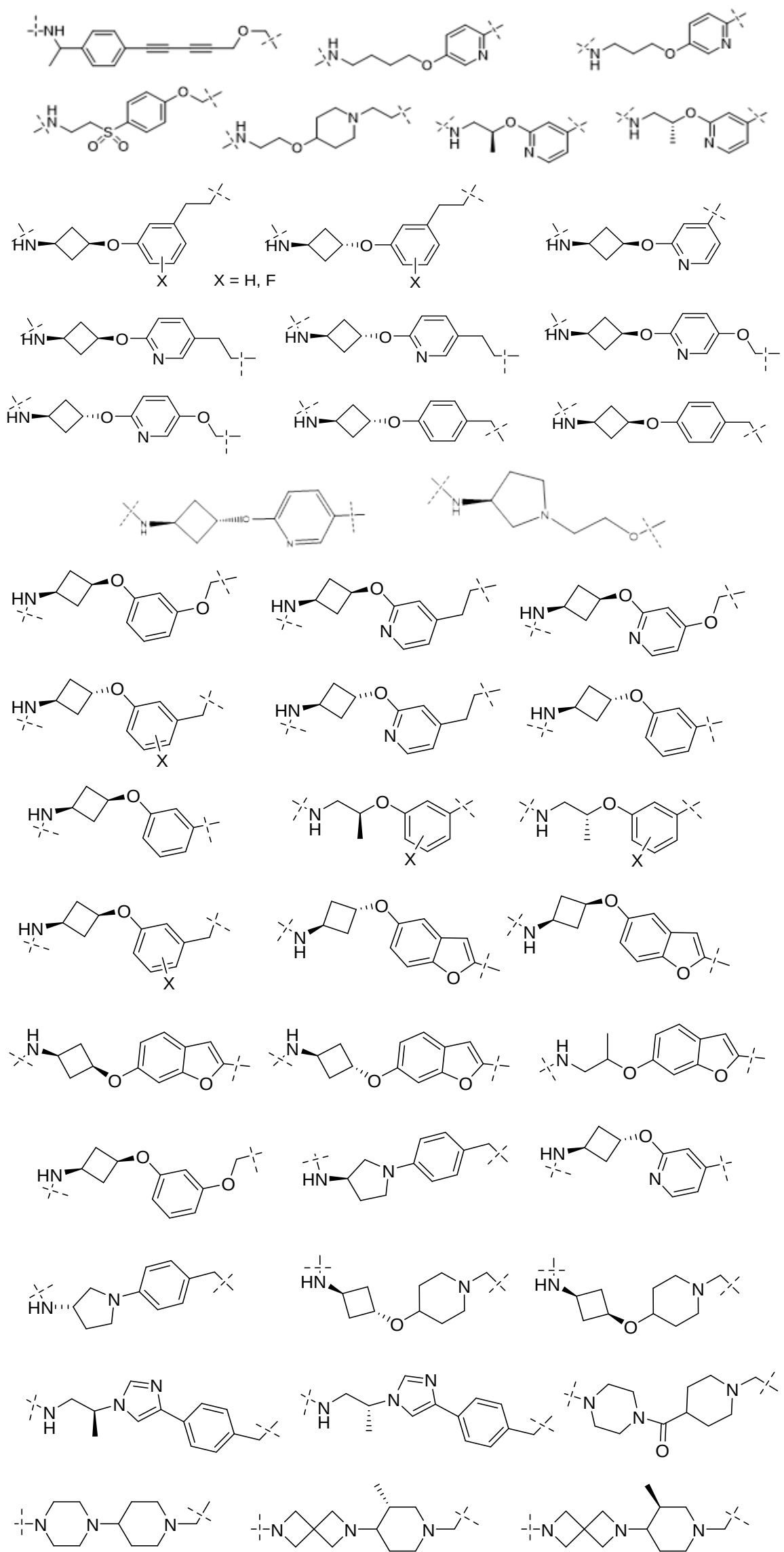
; y

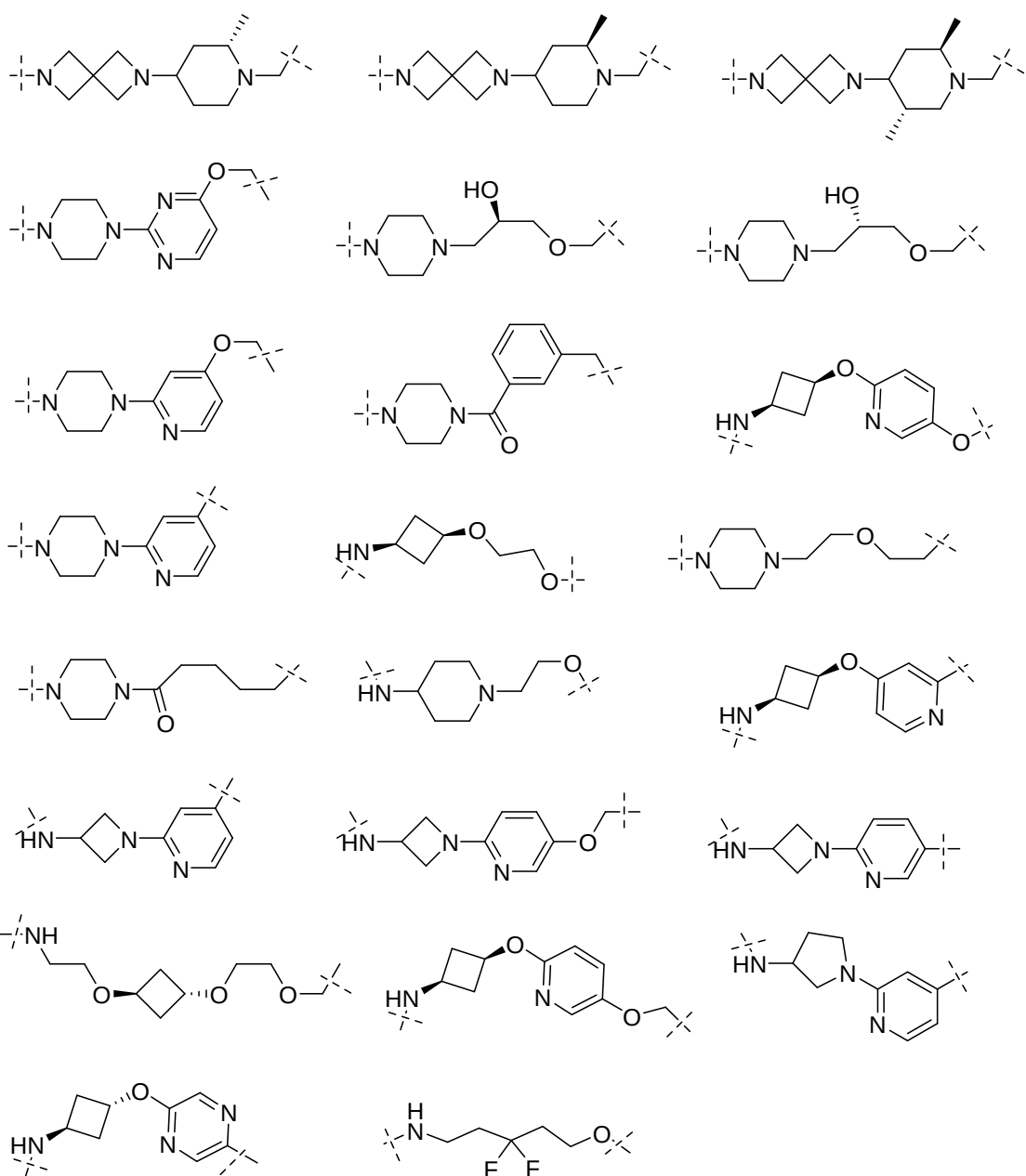


en donde cada m, n, o, p, q, y r, es independientemente 0, 1, 2, 3, 4, 5, o 6, con la salvedad de que cuando el número es cero, no hay enlace N-O o O-O; R se selecciona de H, metilo o etilo, y X se selecciona del grupo H o F;

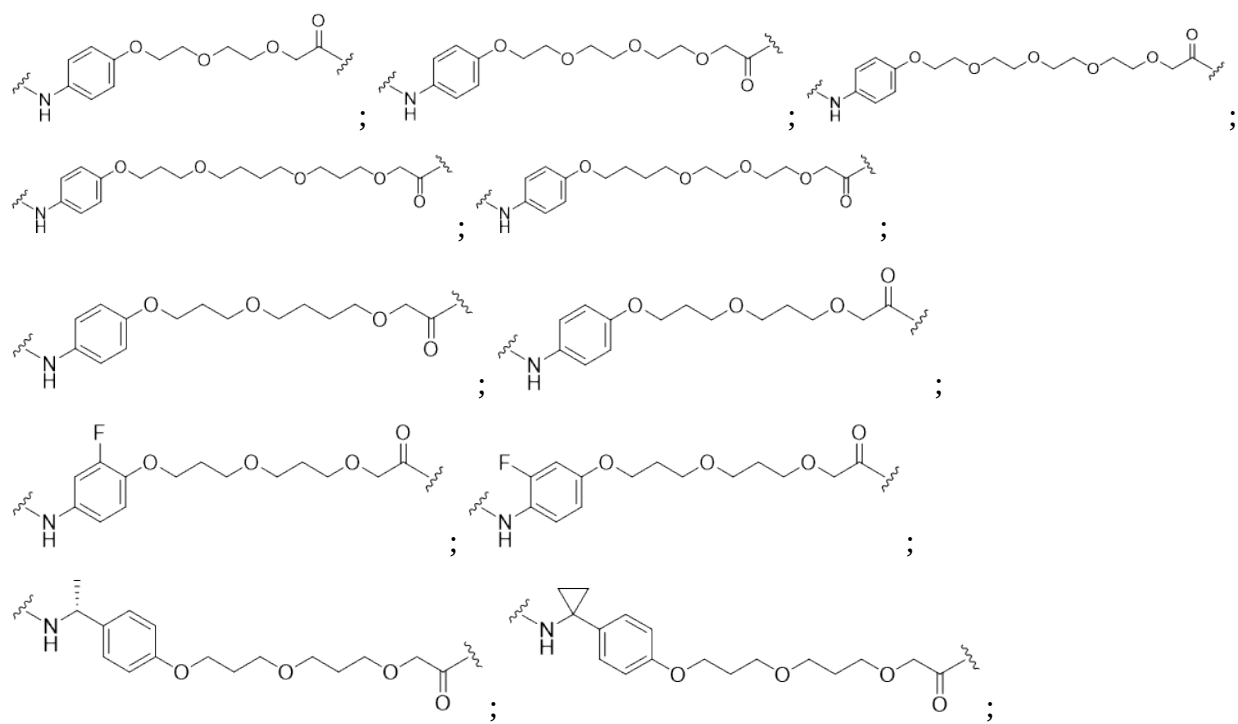


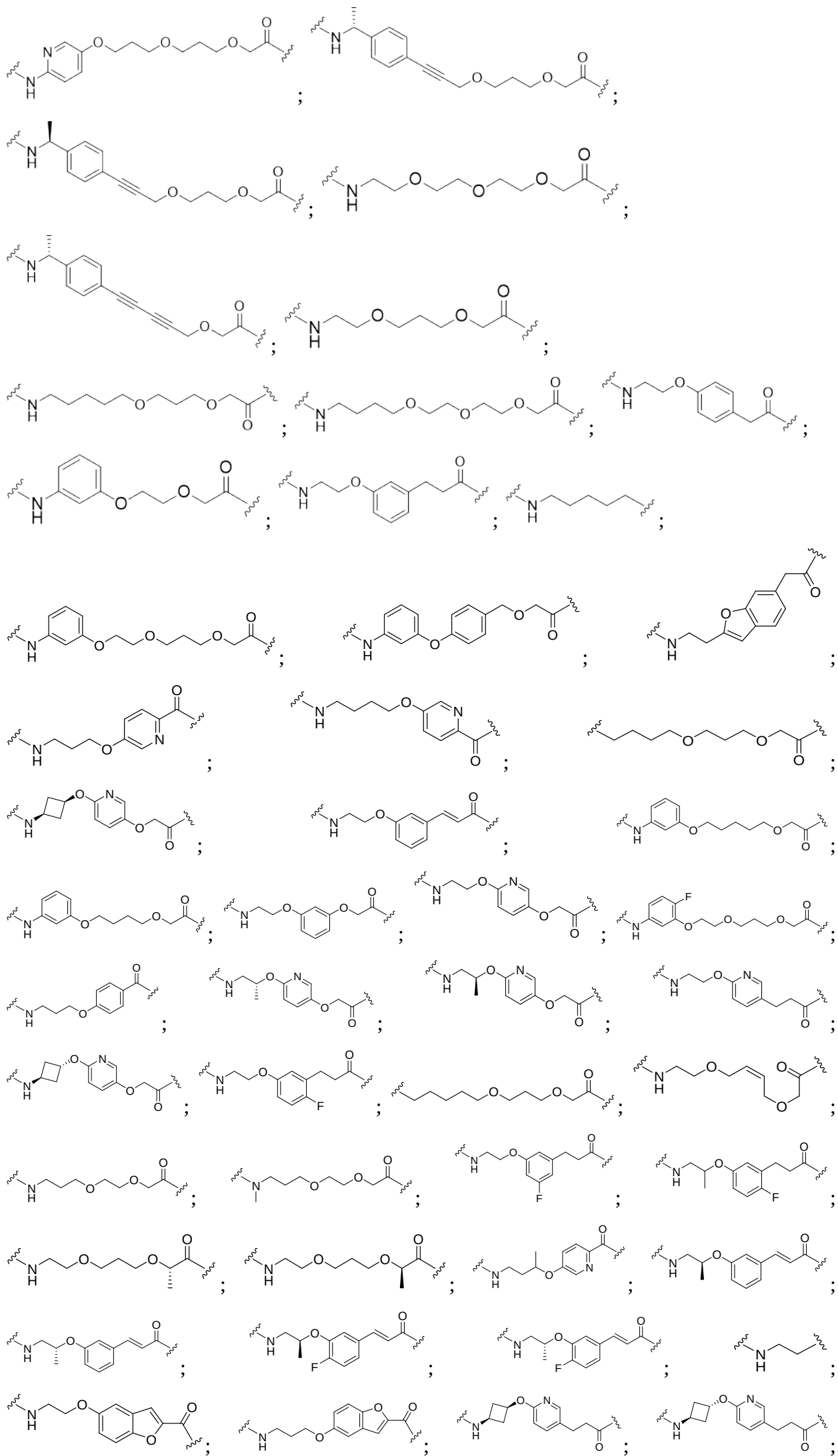


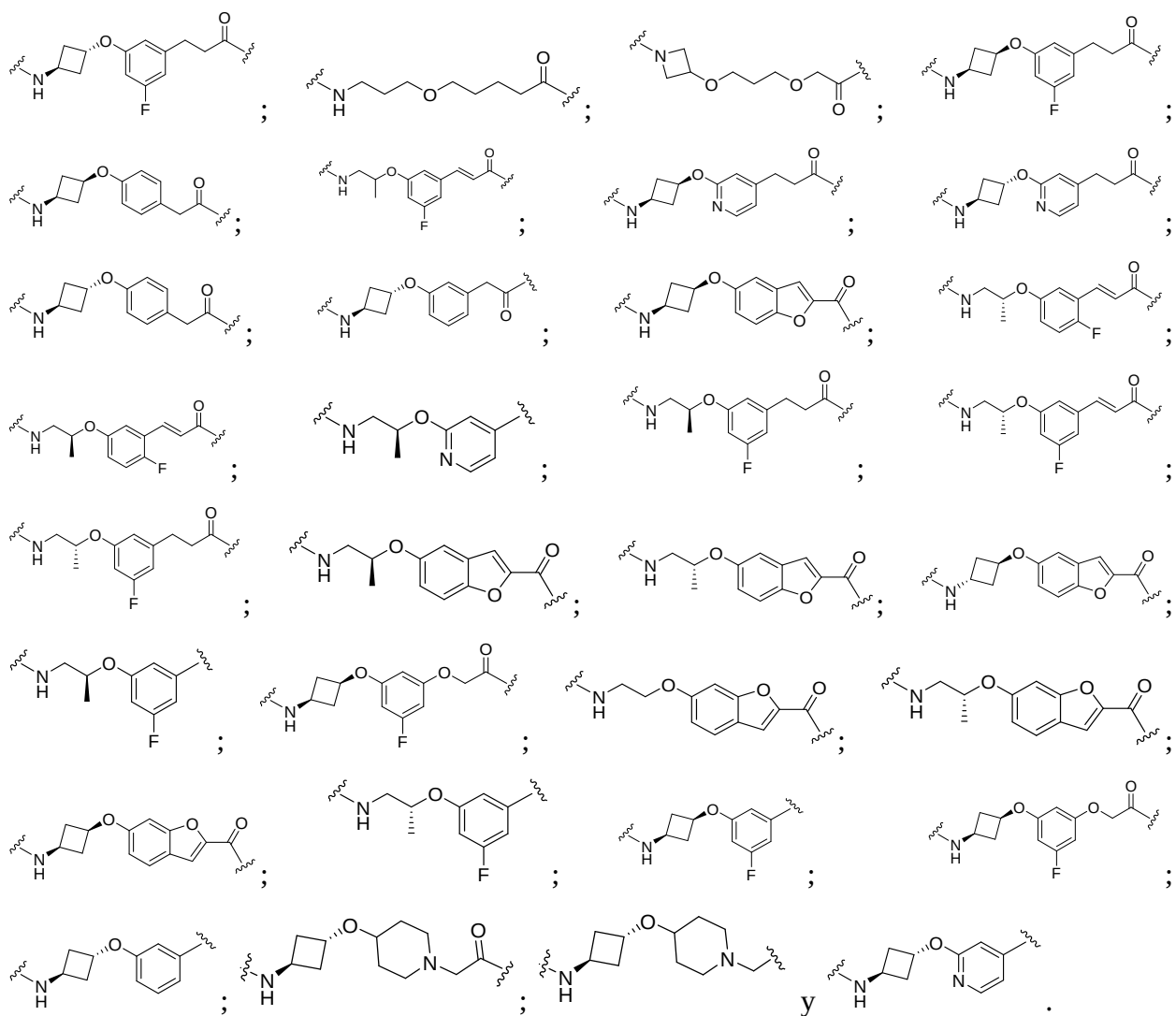




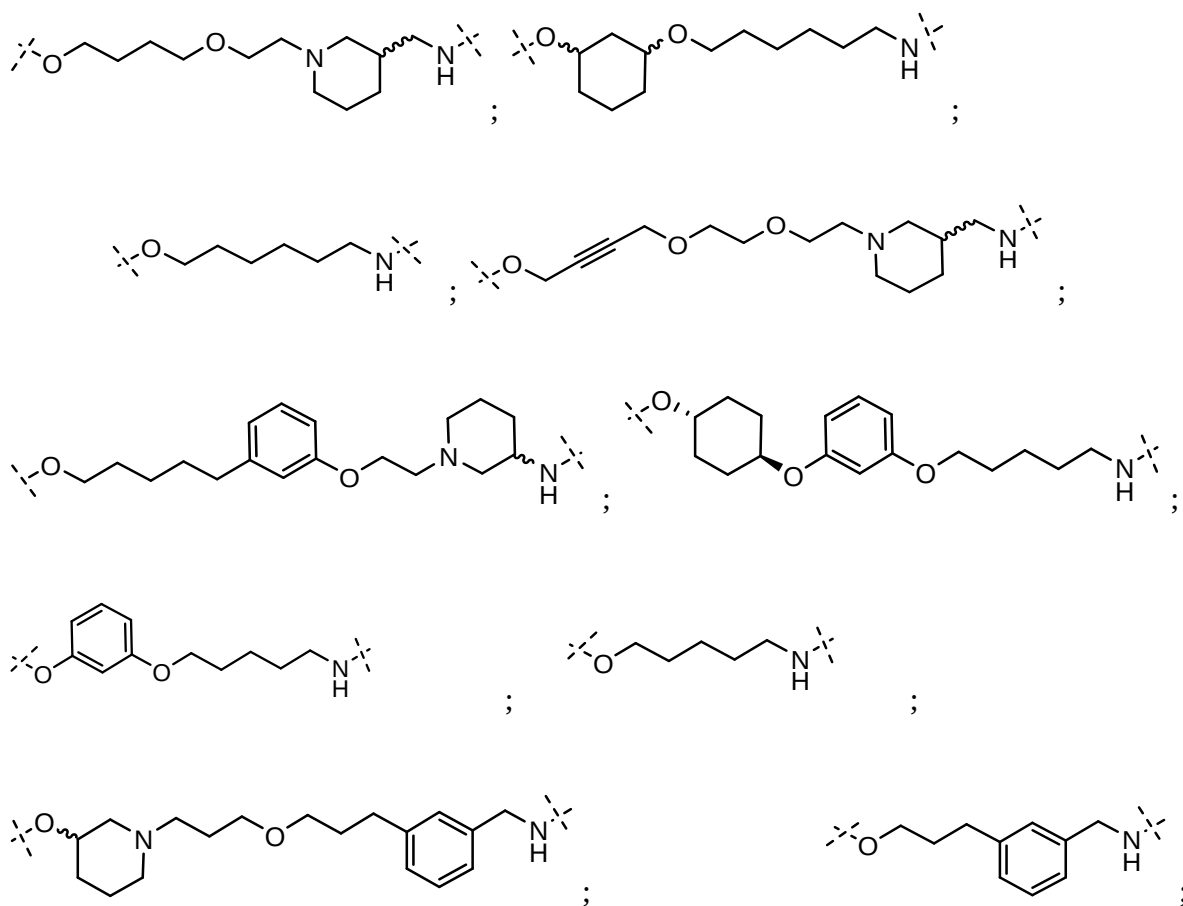
7. El compuesto de conformidad con alguna de las reivindicaciones 1 a 5, en donde el enlazador (L) se selecciona de:

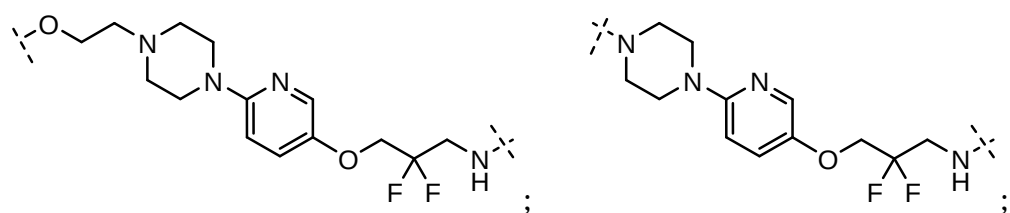
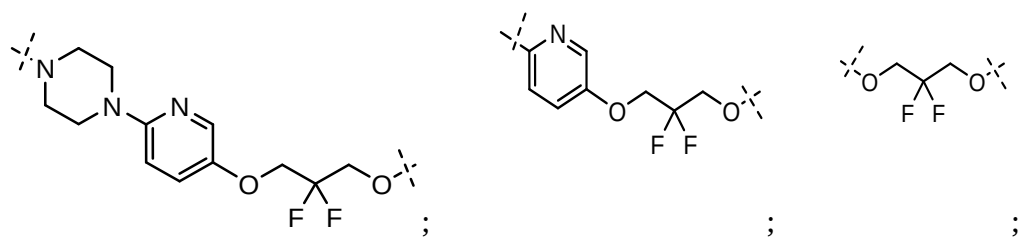
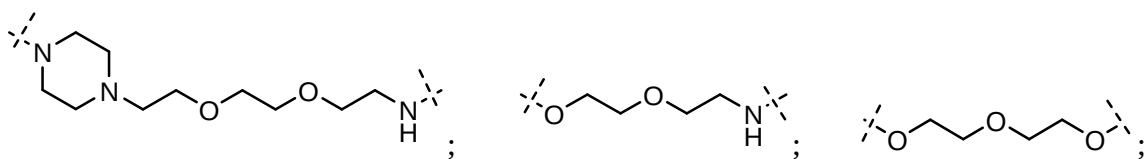
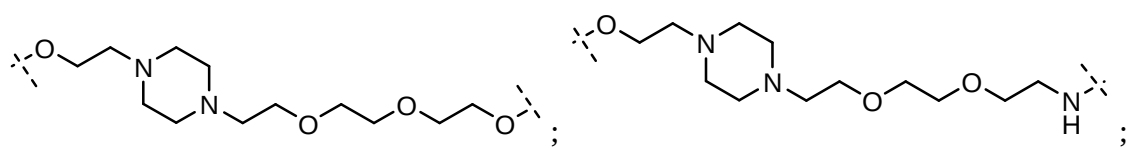
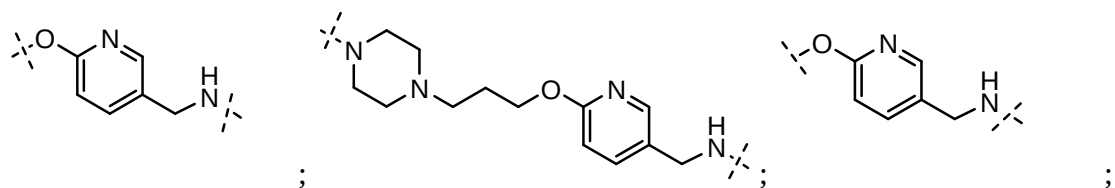
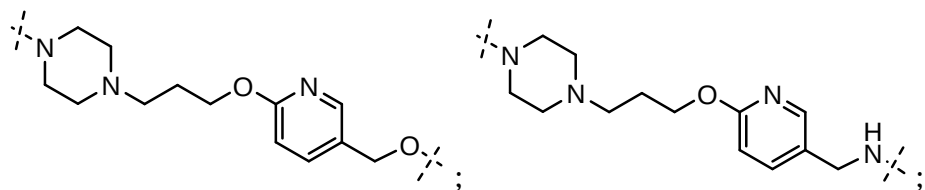
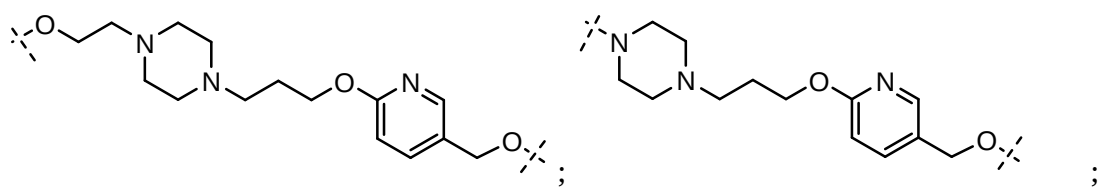
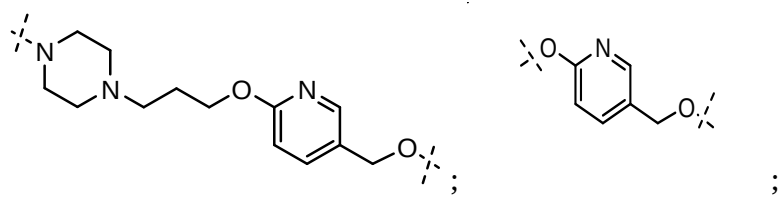


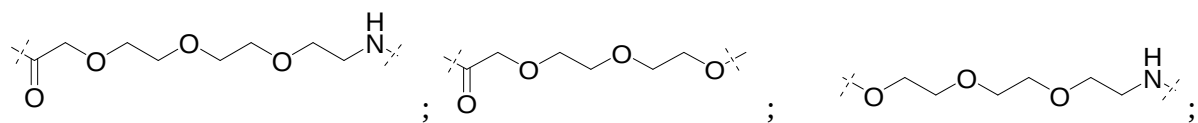
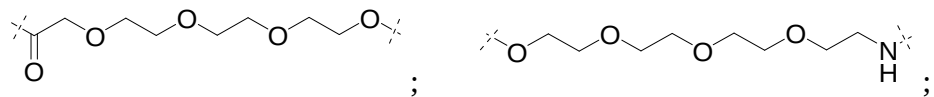
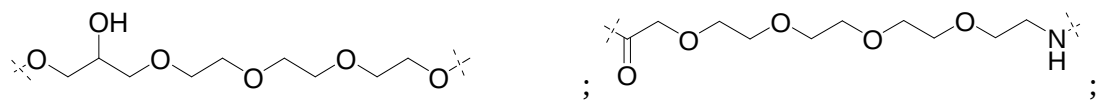
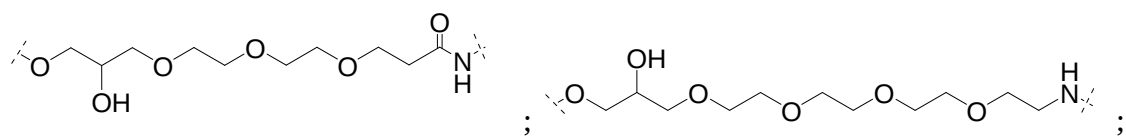
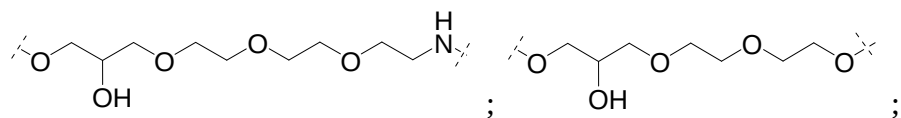
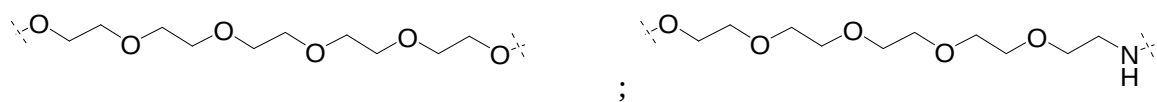
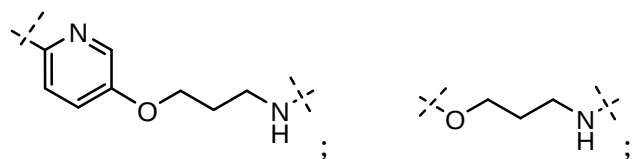
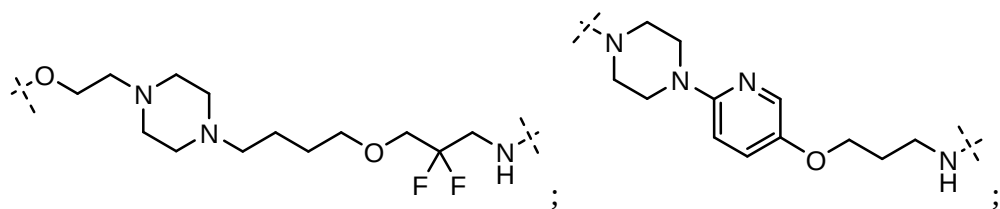
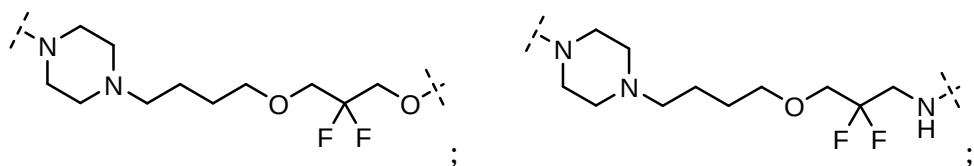
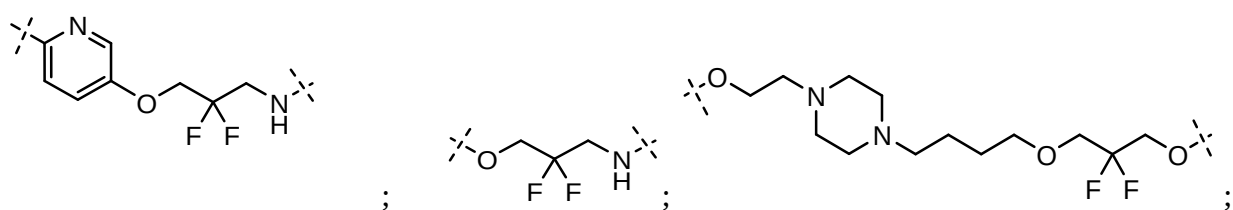


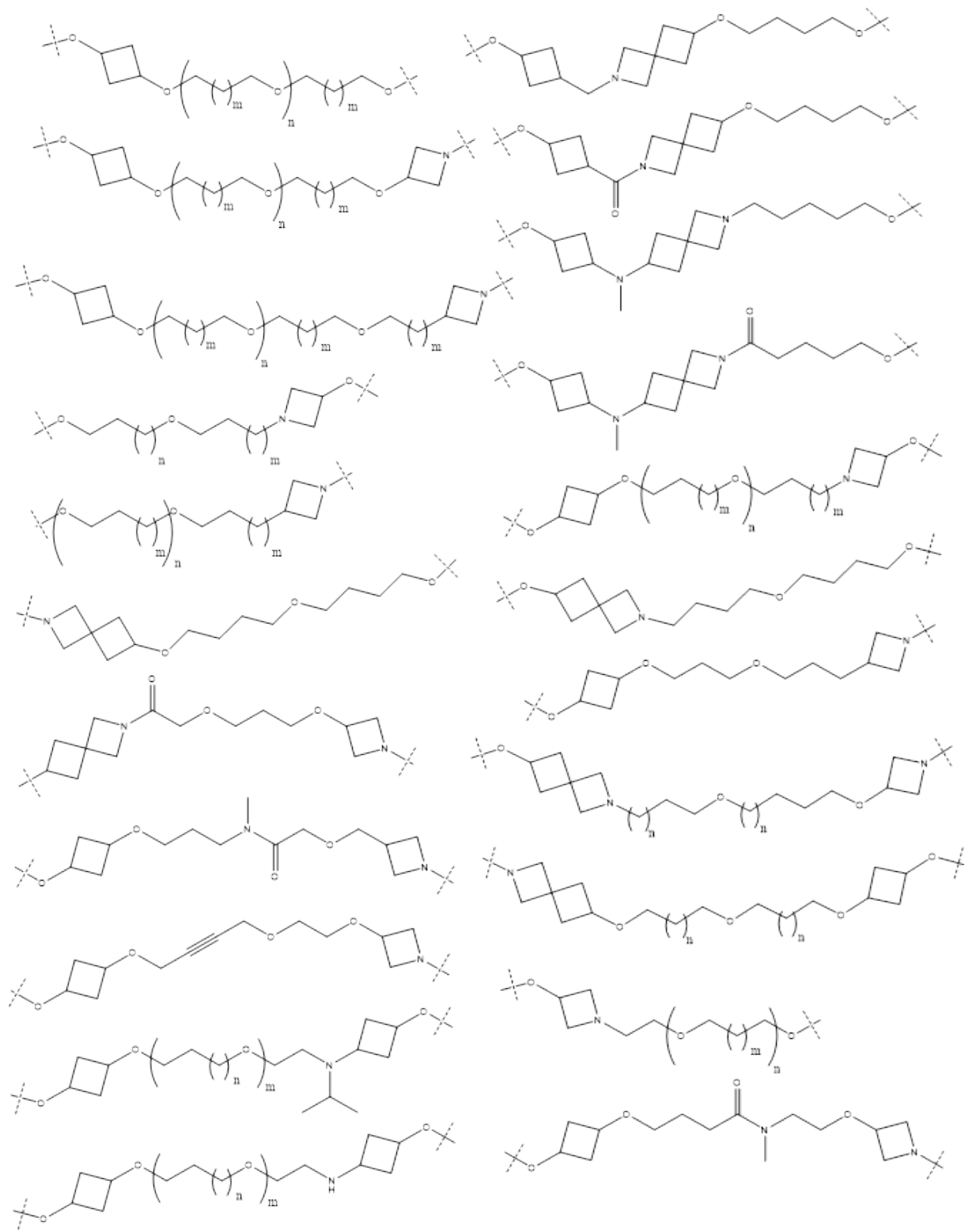


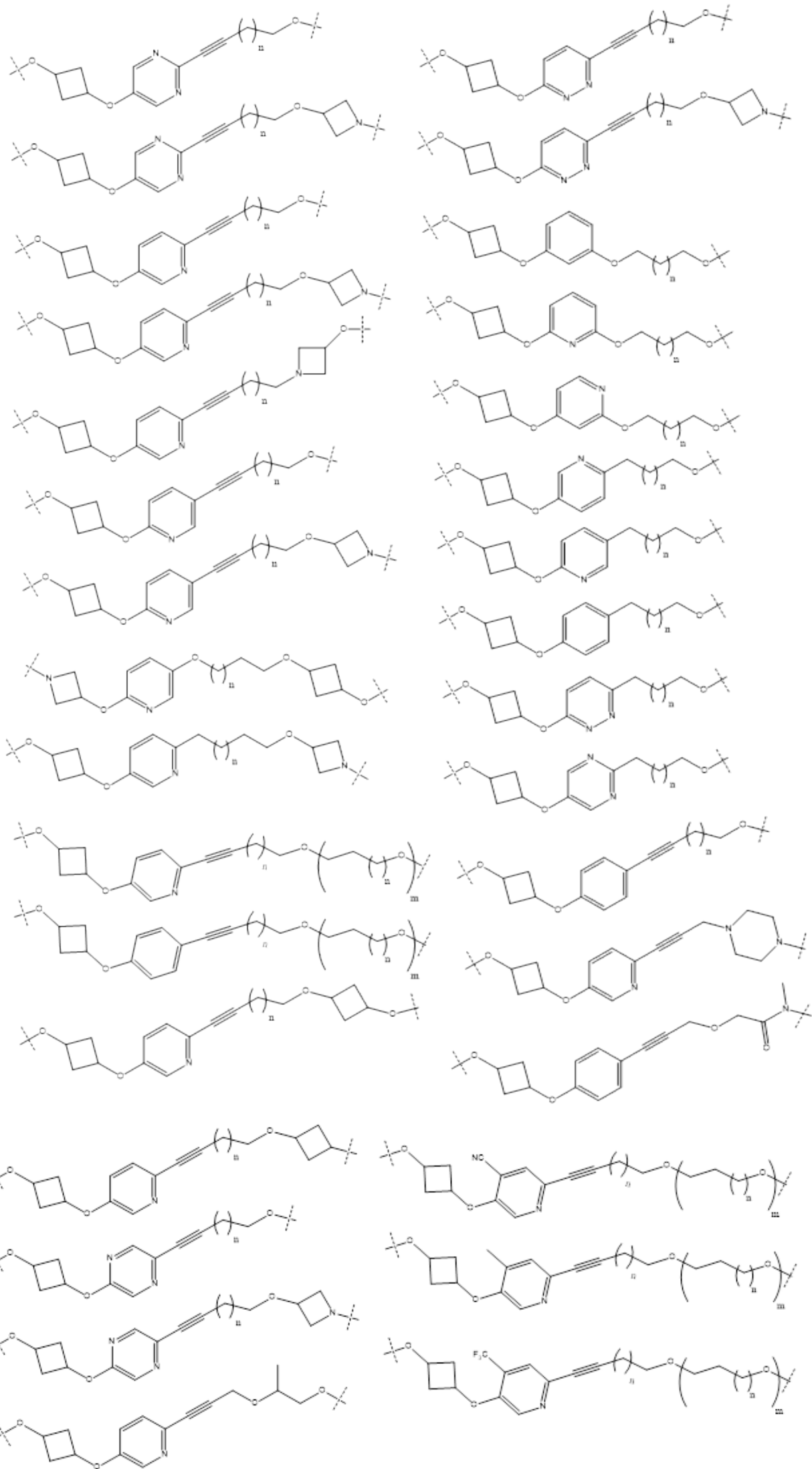
8. El compuesto de conformidad con alguna de las reivindicaciones 1 a 5, en donde el enlazador (L) se selecciona de:

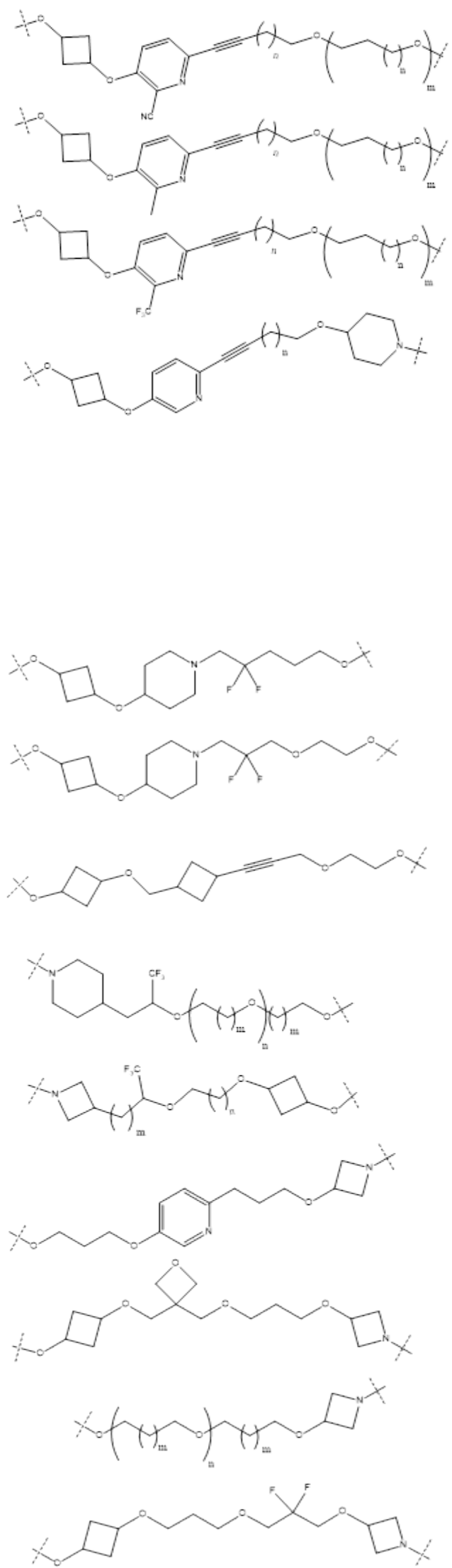


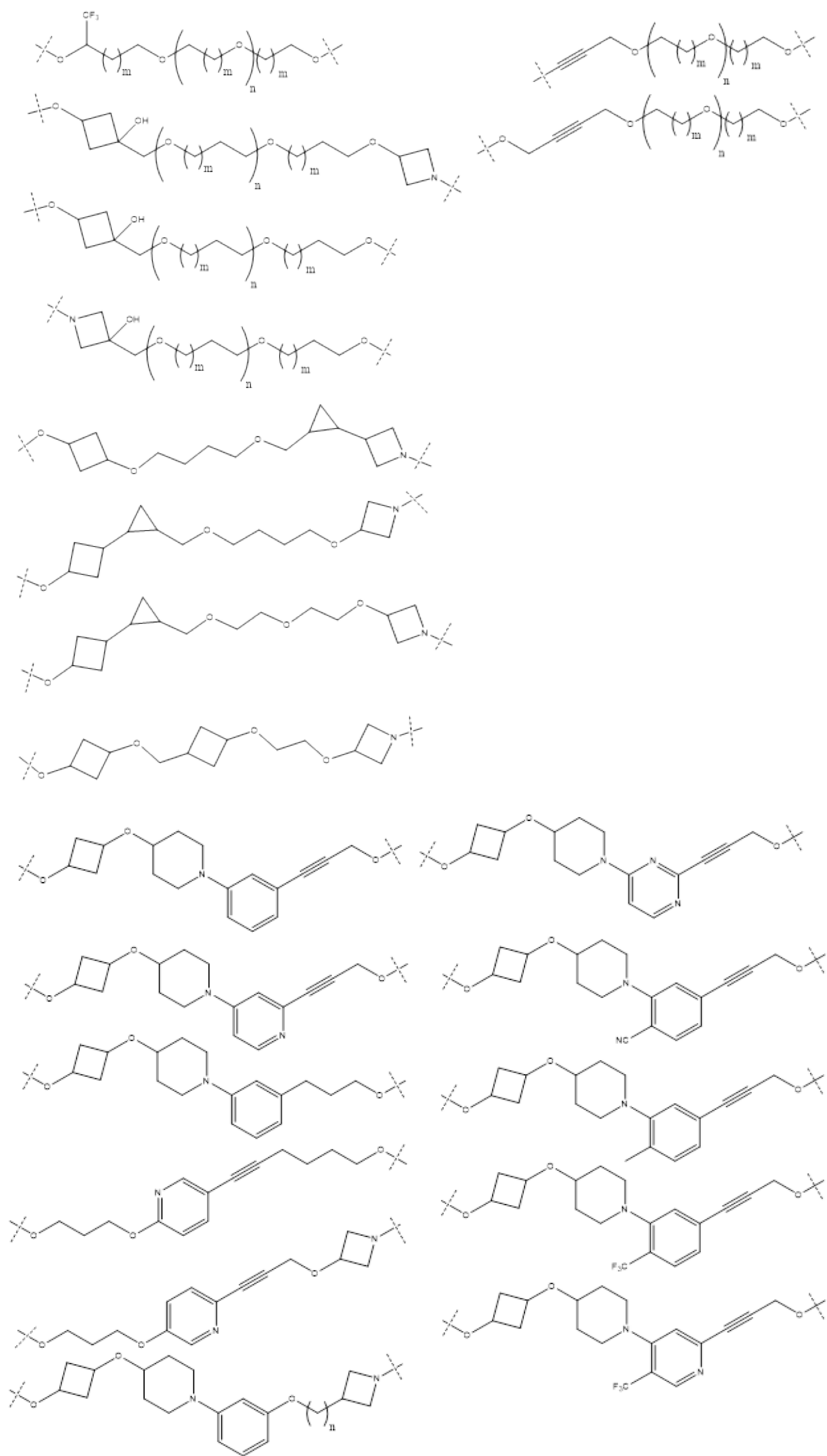


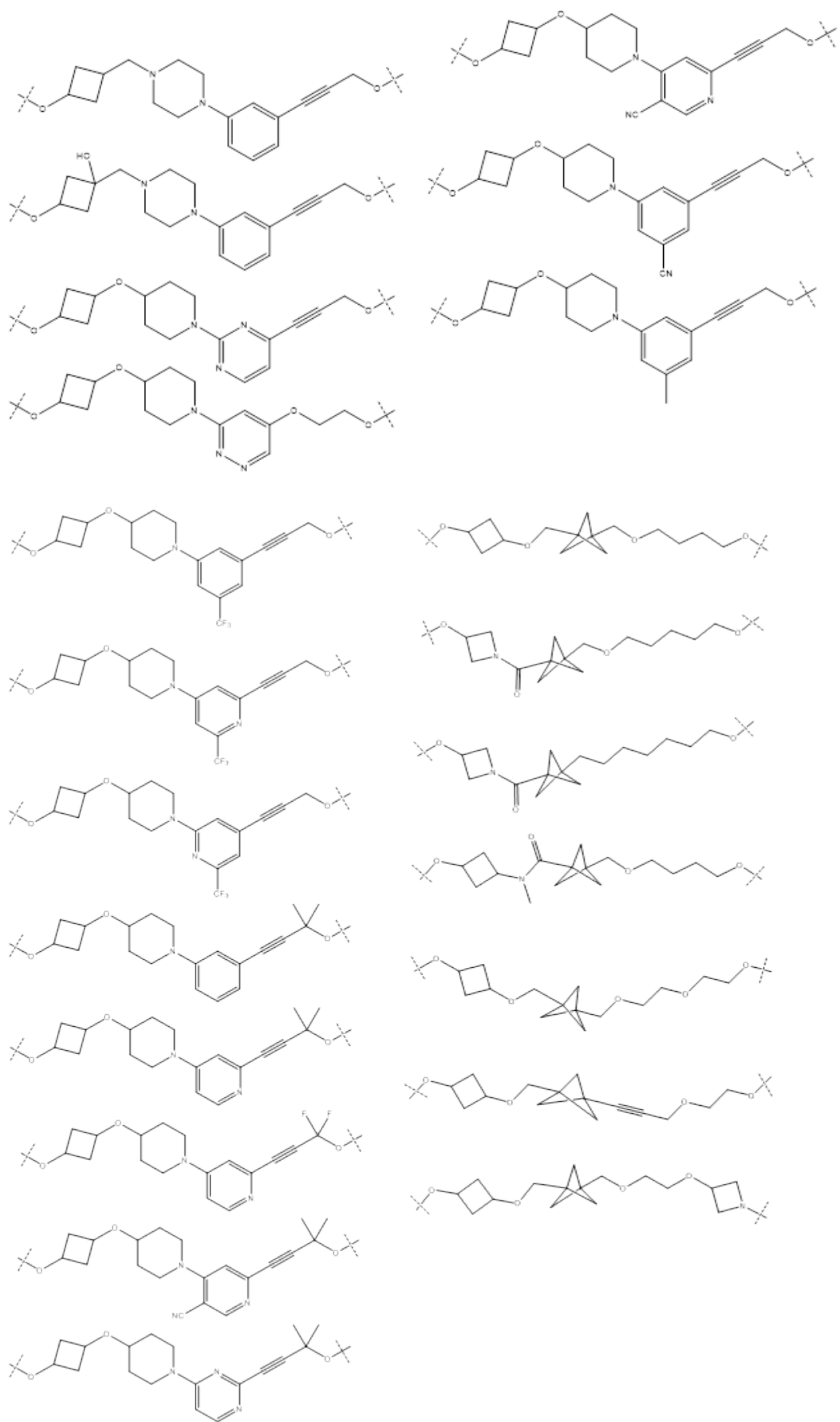


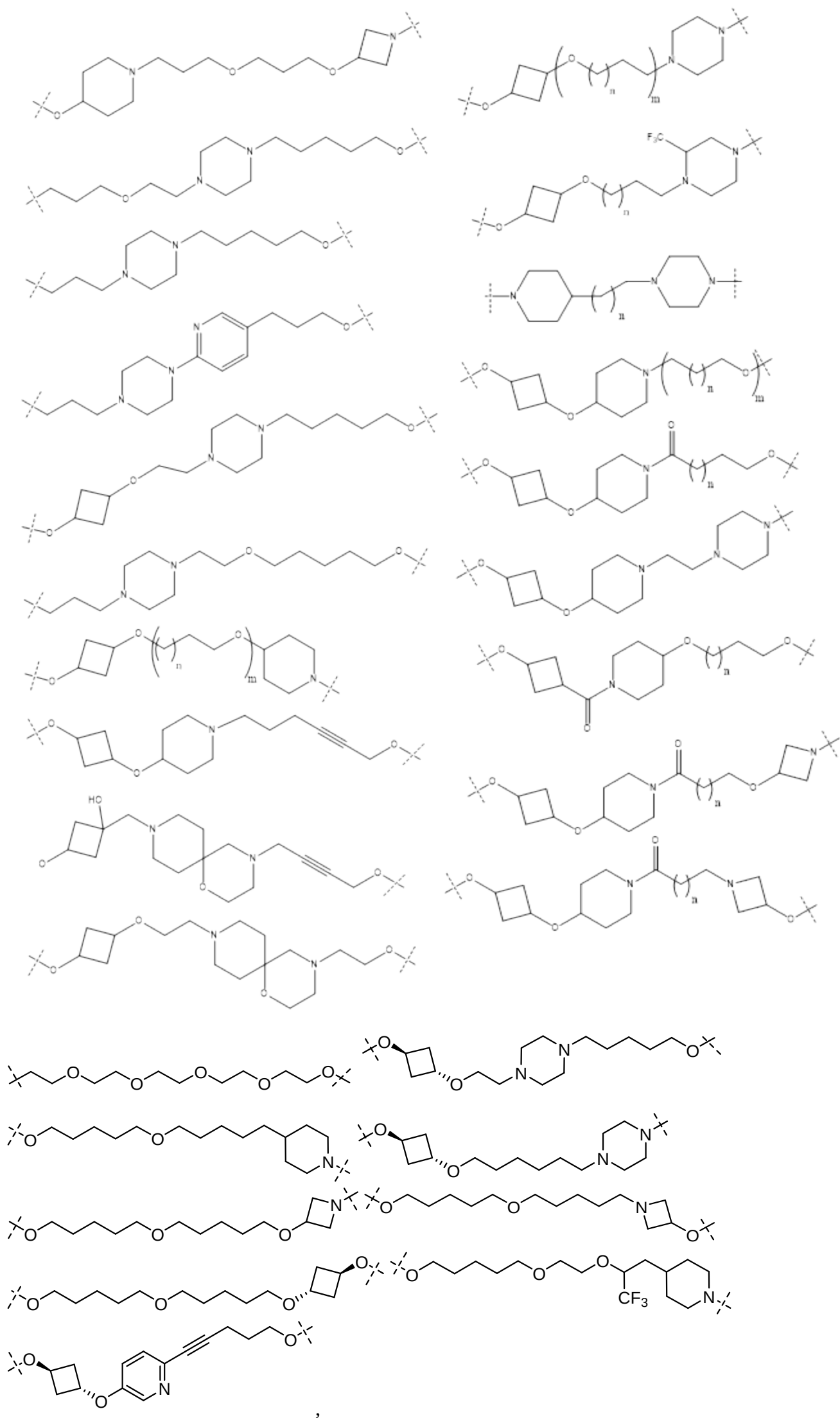






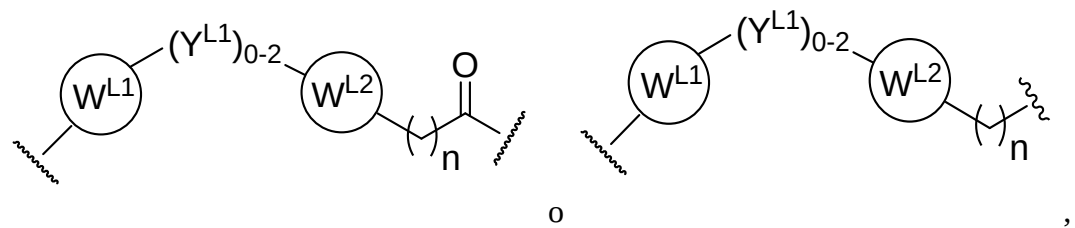






en donde cada n y m es independientemente 0, 1, 2, 3, 4, 5, o 6.

9. El compuesto de conformidad con alguna de las reivindicaciones 1 a 5, en donde el L comprende la siguiente estructura química:



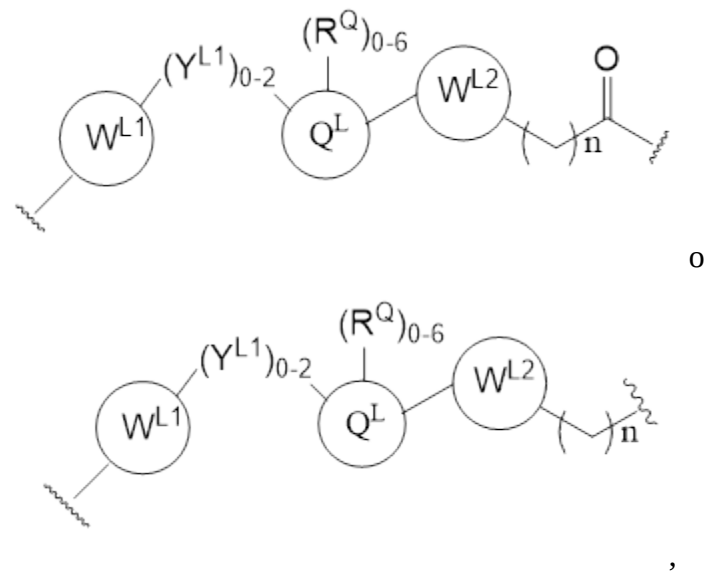
en donde:

$W^{L1}$  y  $W^{L2}$  son cada uno independientemente  $C_6$  arilo, heteroarilo de 5-6 miembros, cicloalquilo de 4-8 miembros, heterocíclico de 4-8, opcionalmente sustituidos con RQ, cada RQ es independientemente un H, halo, OH, CN,  $CF_3$ ,  $C_{1-6}$  alquilo (lineal o ramificado),  $C_{1-6}$  alcoxi (lineal o ramificado), o 2 grupos RQ tomados juntos con el átomo al que se unen para, formar  $C_{4-8}$  cicloalquilo o heterociclilo de 4-8 miembros;

cada  $Y^{L1}$  es independientemente un enlace,  $C_{1-6}$  alquilo lineal o ramificado opcionalmente sustituido con 1-3 halógenos y opcionalmente uno o más átomos de C se reemplazan con O; y

una línea discontinua indica el punto de acoplamiento a PTM o ULM.

10. El compuesto de conformidad con alguna de las reivindicaciones 1 a 5, en donde L comprende la siguiente estructura química:



en donde:

$W^{L1}$  y  $W^{L2}$  son cada uno independientemente arilo de  $C_{6-10}$ , heteroarilo de 6-10 miembros, cicloalquilo de 3-11 miembros, heterocíclico de 3-10 miembros, o alquilo de  $C_{1-6}$ , cada uno opcionalmente sustituido con  $R^Q$ , cada  $R^Q$  es independientemente halo, OH, CN,  $CF_3$ , hidroxilo,  $C_{1-6}$  alquilo (lineal o ramificado),  $C_{1-6}$  alcoxi (lineal o ramificado),  $NH_2$ , o  $NR^{Y1}R^{Y2}$ , o 2 grupos  $R^Q$  tomados juntos con el átomo al que se unen para, formar  $C_{4-8}$  cicloalquilo o heterociclilo de 4-8 miembros;

cada  $Y^{L1}$  es independientemente un enlace,  $NR^{YL1}$ , O, S,  $CR^{YL1}R^{YL2}$ , C=O, SO, SO<sub>2</sub>, C<sub>1-6</sub> alquilo (lineal o ramificado) y opcionalmente uno o más átomos de C se reemplazan con O;

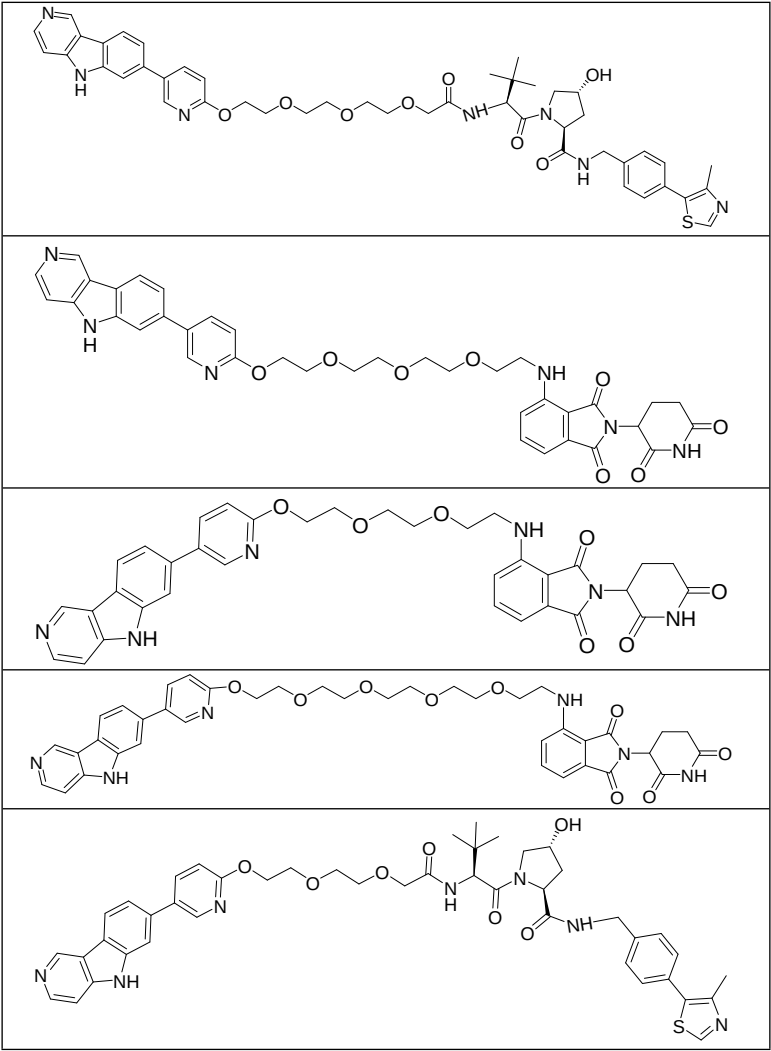
$Q^L$  es un C<sub>3-6</sub> cicloalquilo, heterociclilo de 3-6 miembros, C<sub>6</sub> arilo, o heteroarilo de 5-6 miembros, opcionalmente sustituido con 1 o 2  $R^Q$ , cada  $R^Q$  es independientemente H, alquilo de C<sub>1-6</sub> opcionalmente sustituido por 1 o más halo o alcoxi de C<sub>1-6</sub>, o 2 grupos  $R^Q$  tomados juntos con el átomo al que se unen para, formar C<sub>3-8</sub> cicloalquilo y/o heterociclilo de 3-8 miembros;

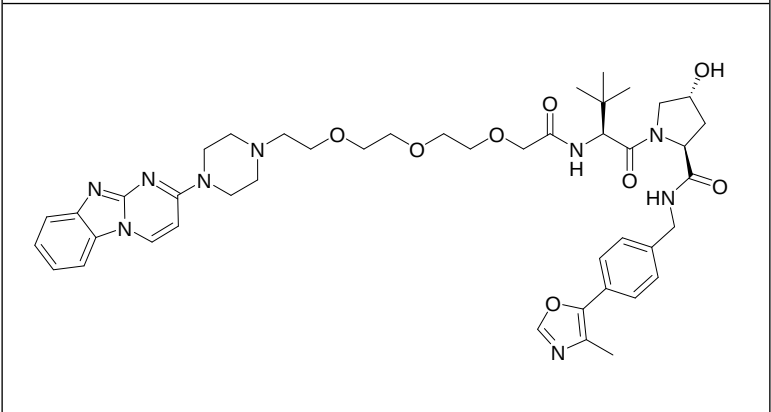
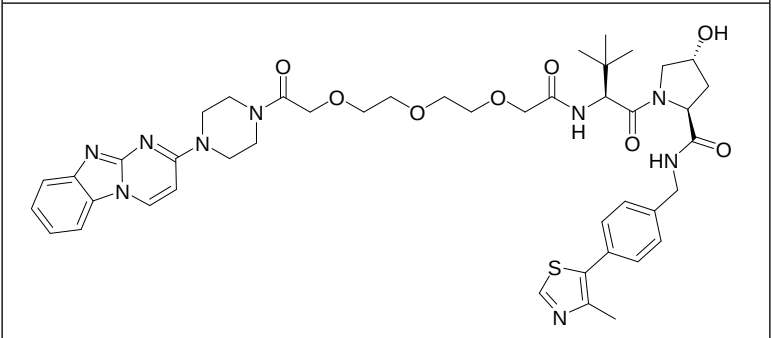
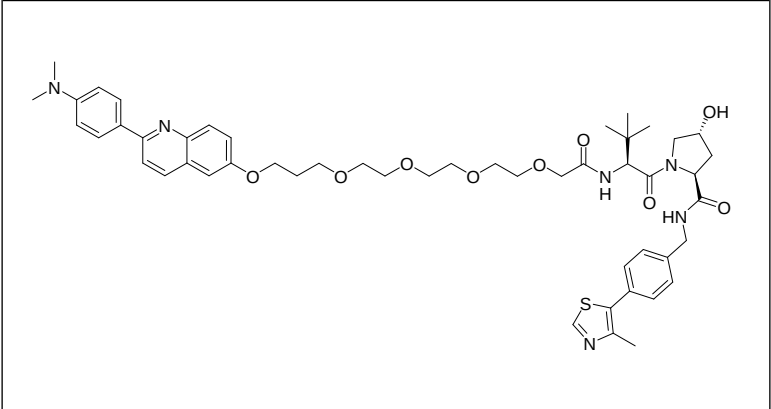
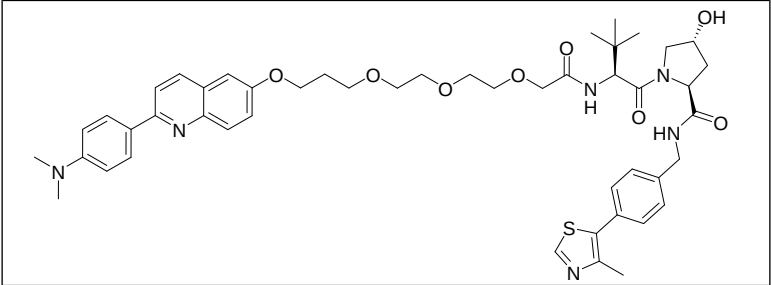
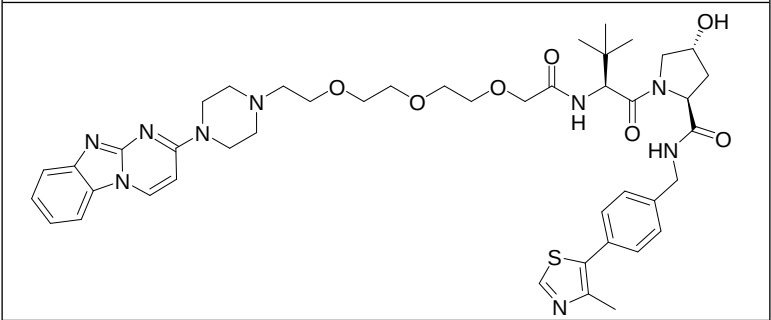
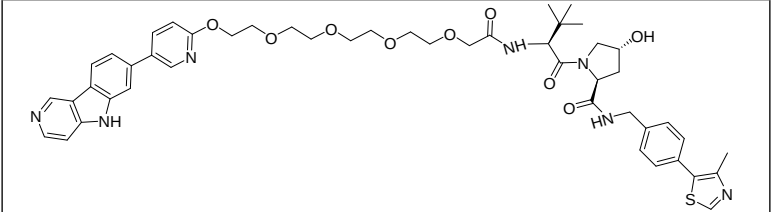
$R^{YL1}$  y  $R^{YL2}$  son cada uno independientemente H, OH, alquilo de C<sub>1-6</sub> lineal o ramificado, opcionalmente sustituido por 1 o más halo o alcoxi de C<sub>1-6</sub>;

n es 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, o 10; y

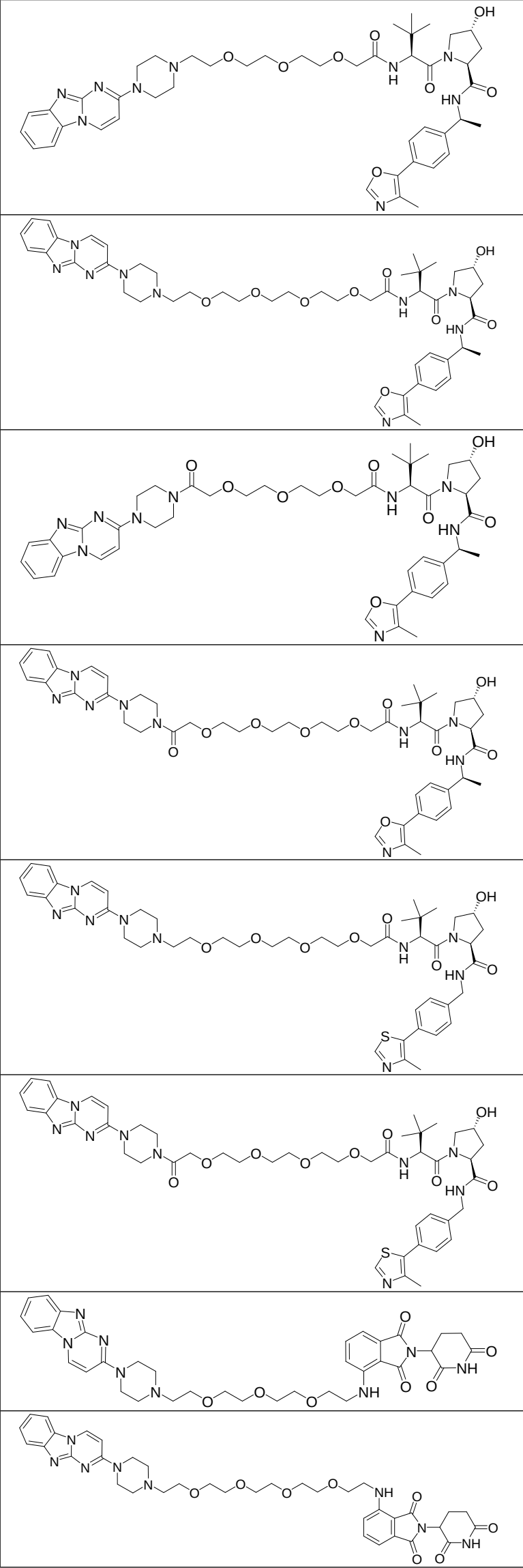
una línea discontinua indica el punto de acoplamiento a PTM o ULM.

- 11. El compuesto de conformidad con alguna de las reivindicaciones 1 a 5, en donde el L es un grupo polietilenoxi opcionalmente sustituido con arilo de C<sub>6-10</sub> que comprende de 1 a 10 unidades de etilenglicol.
- 12. El compuesto bifuncional de alguna de las reivindicaciones 1 a 11, en donde el compuesto se selecciona de:

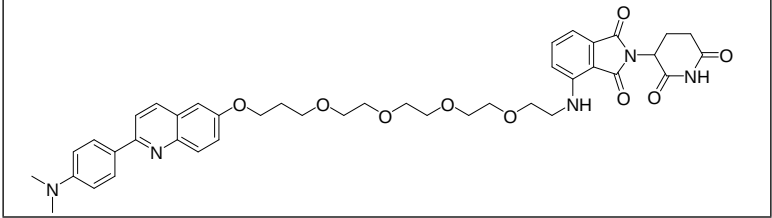
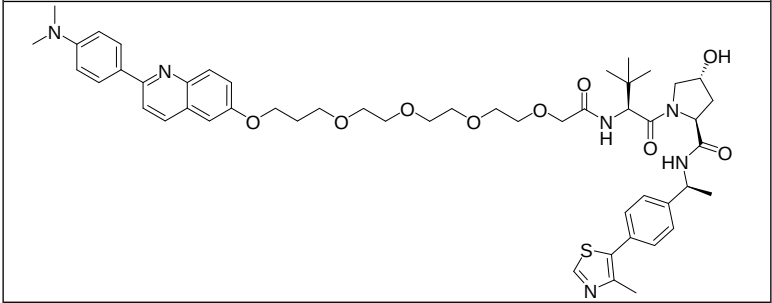
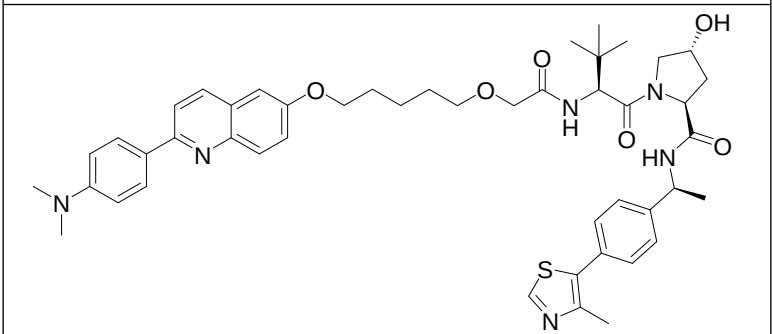
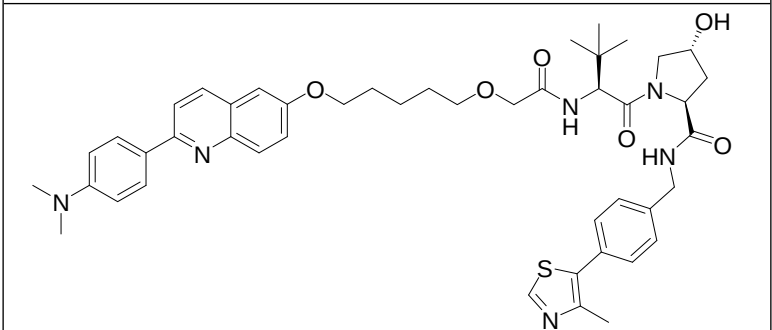
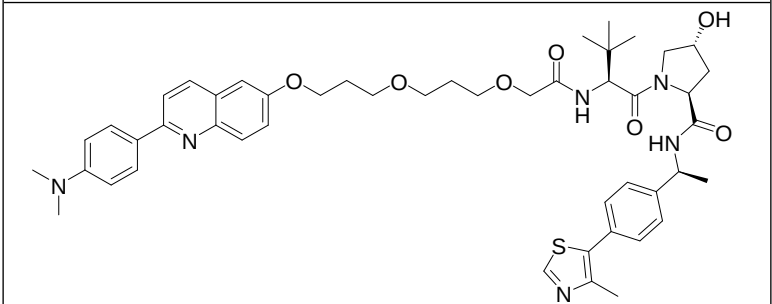
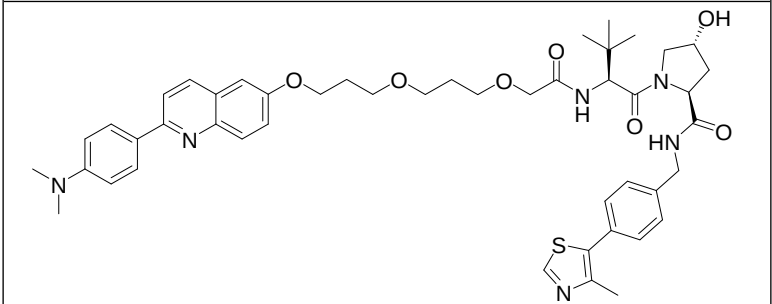
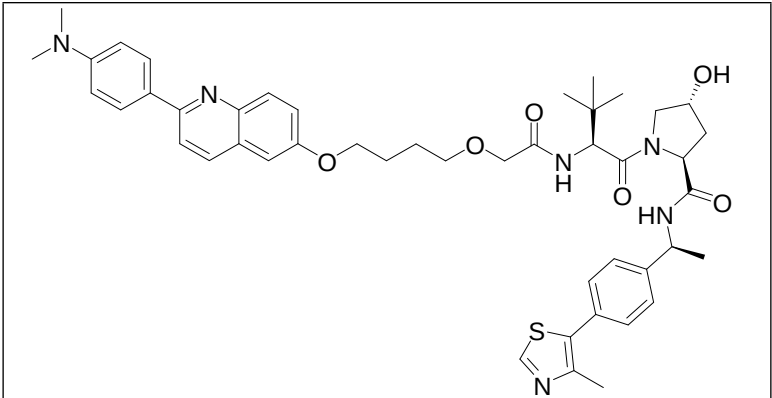




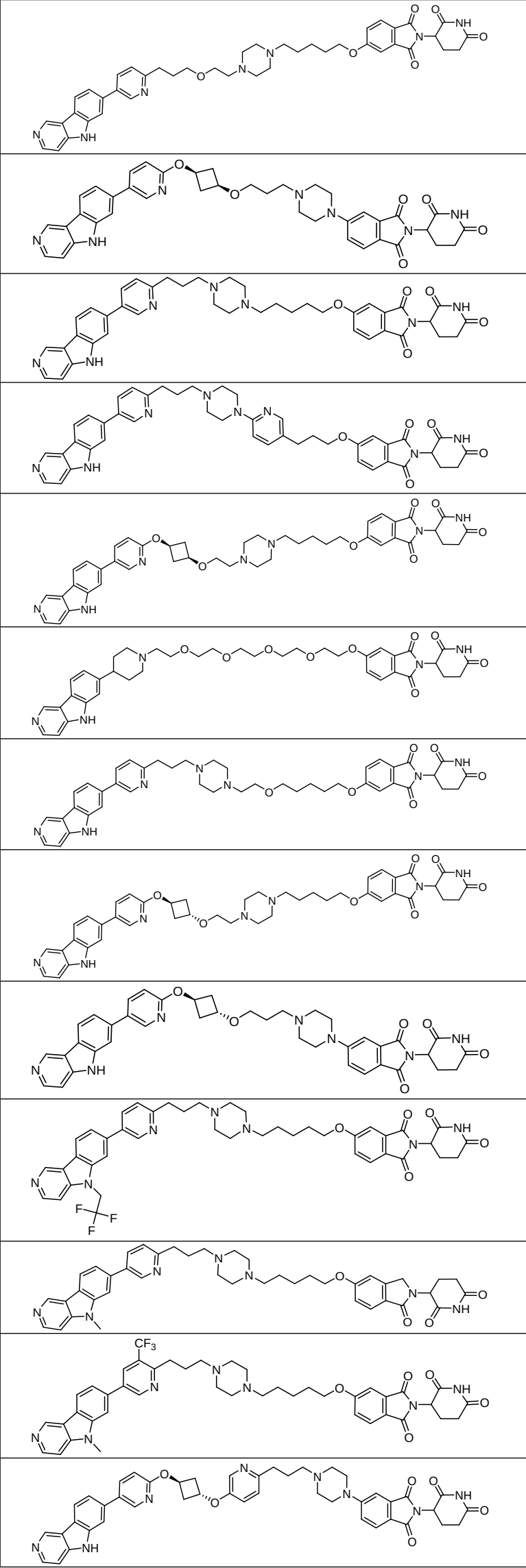


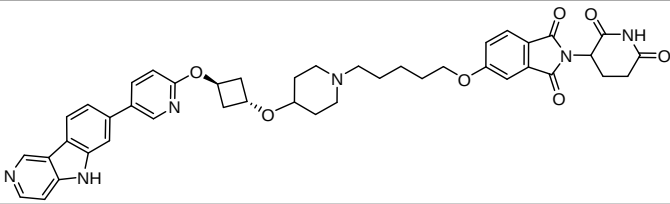
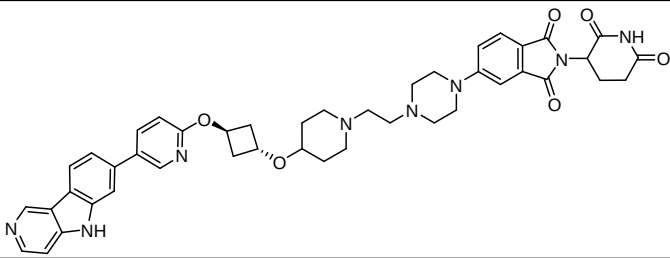
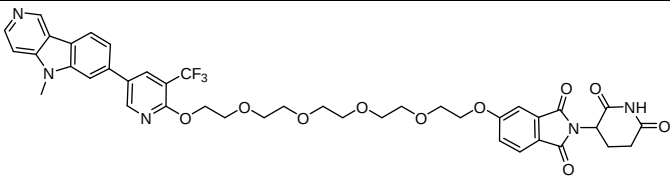
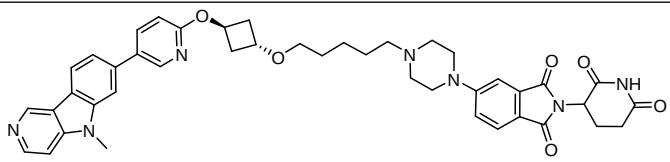
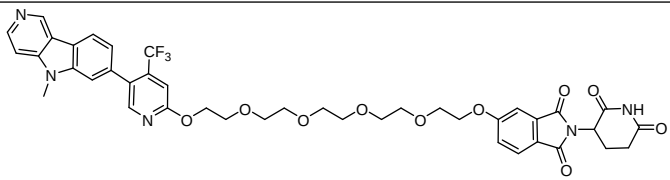
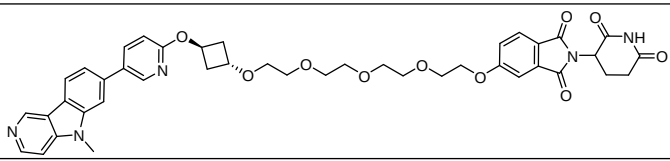
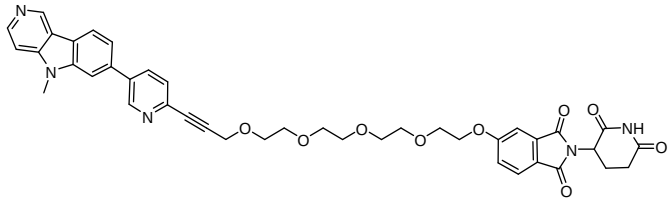
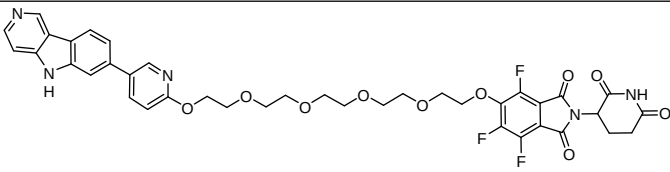
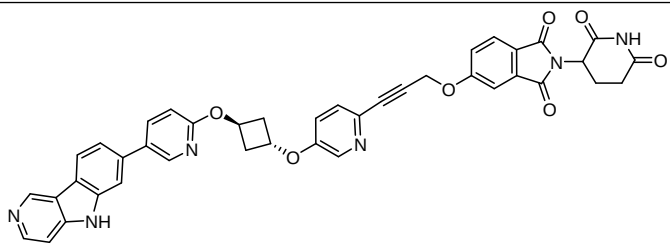
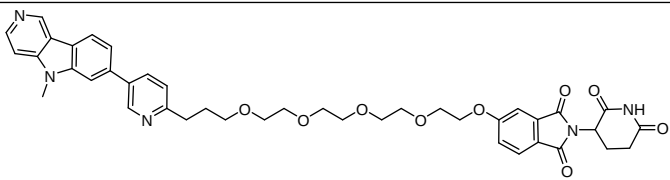
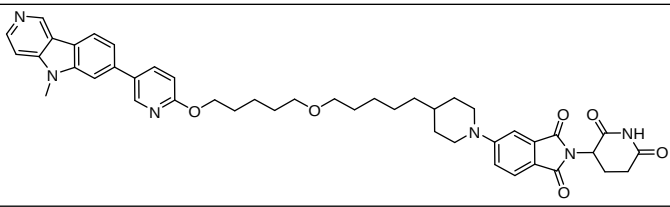


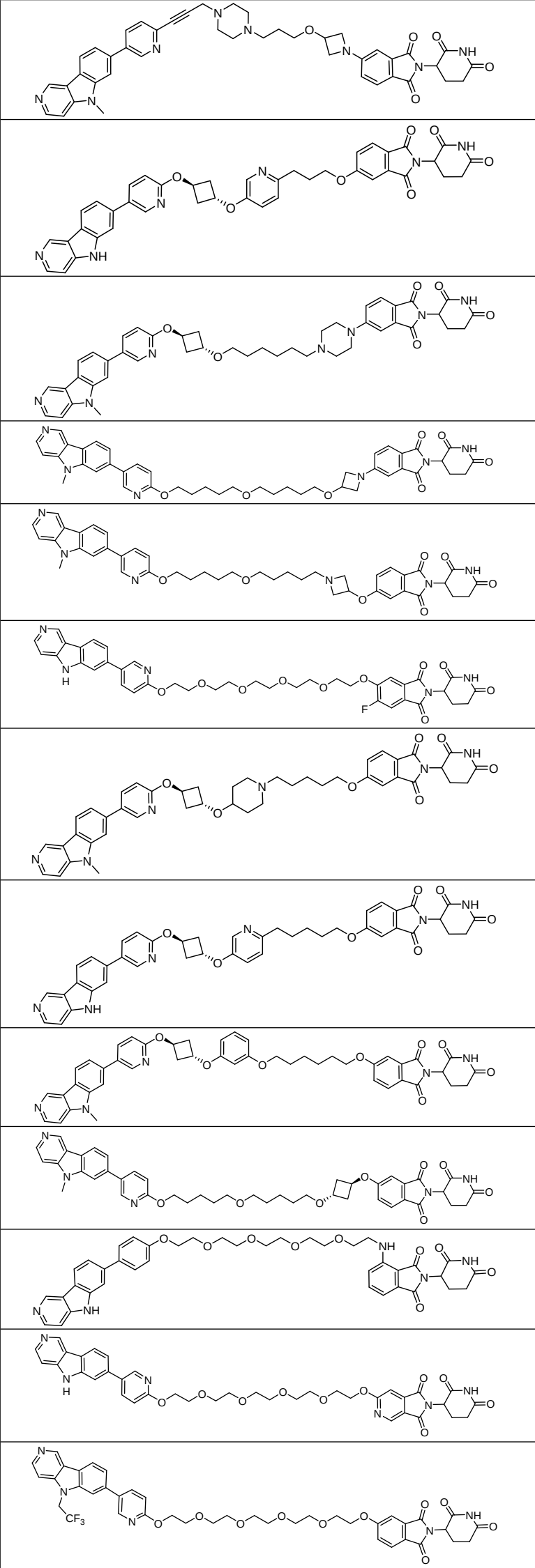


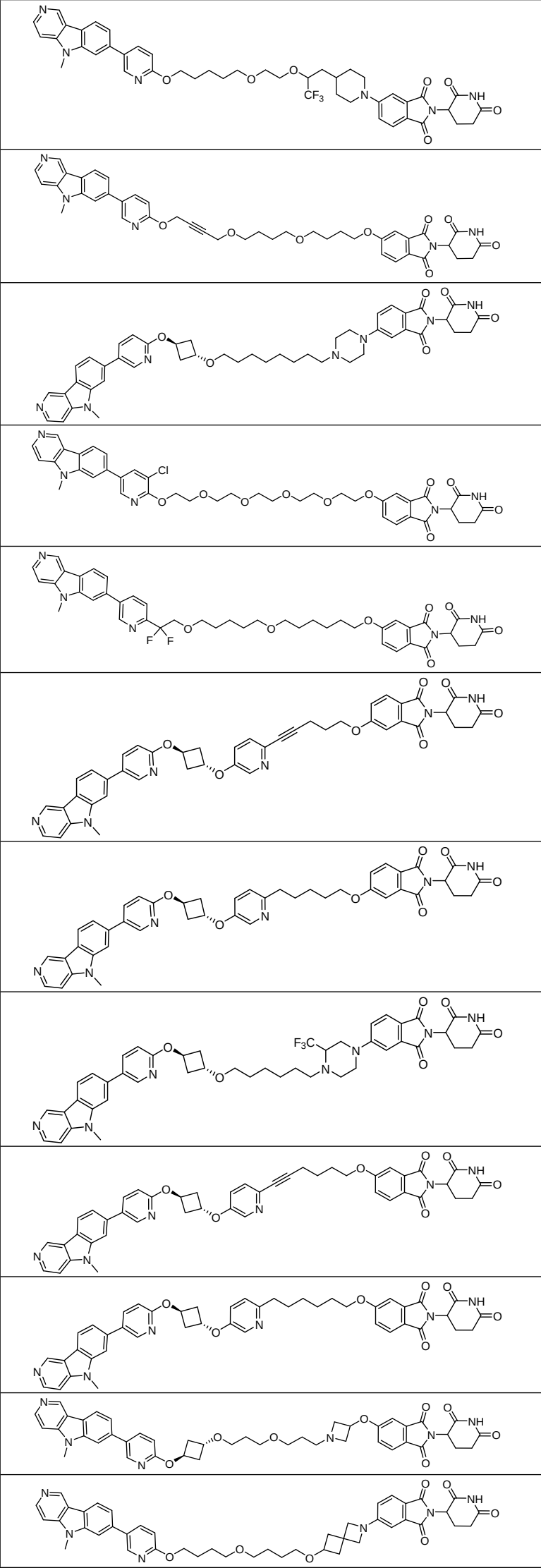


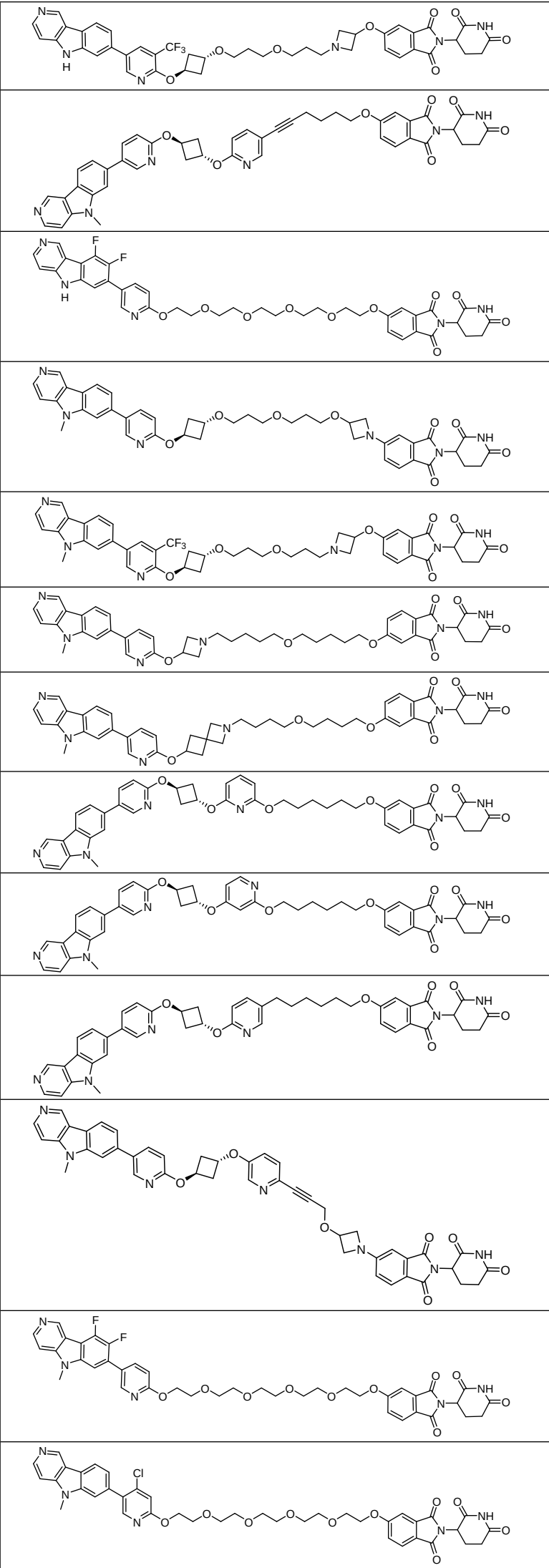


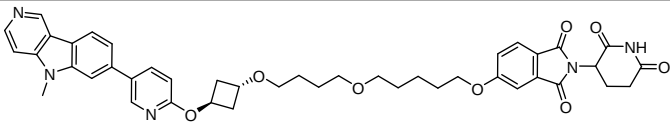
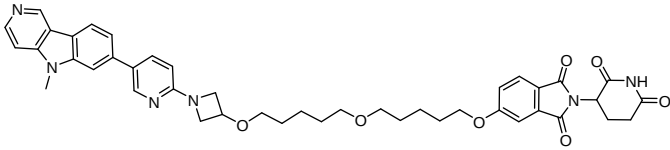
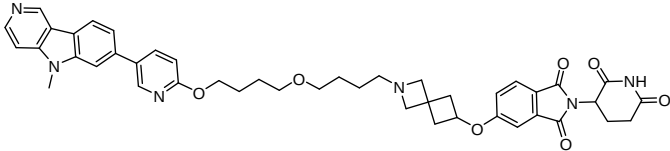
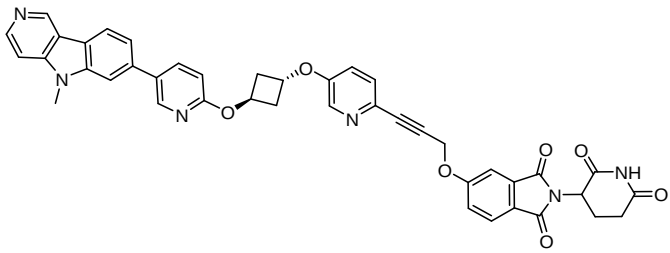
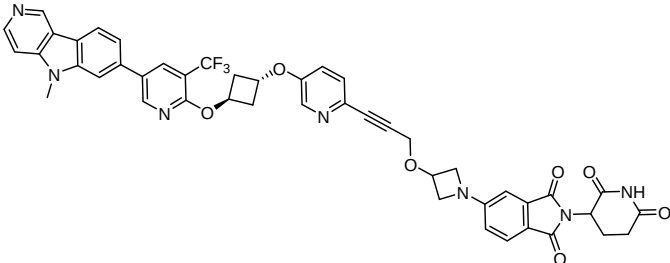
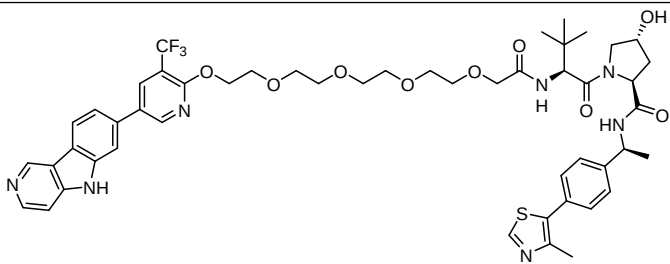
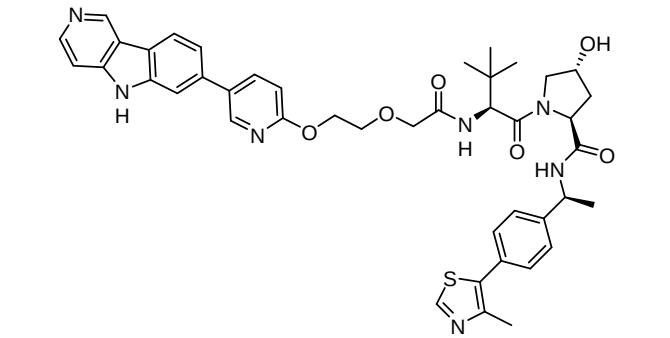
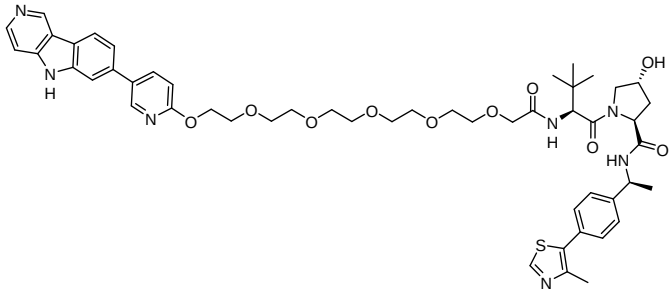
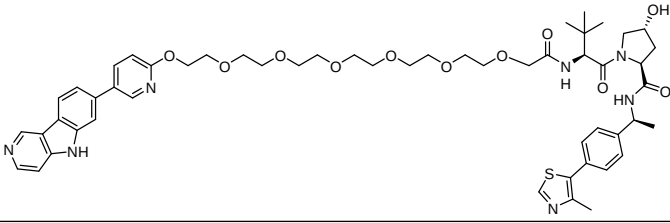


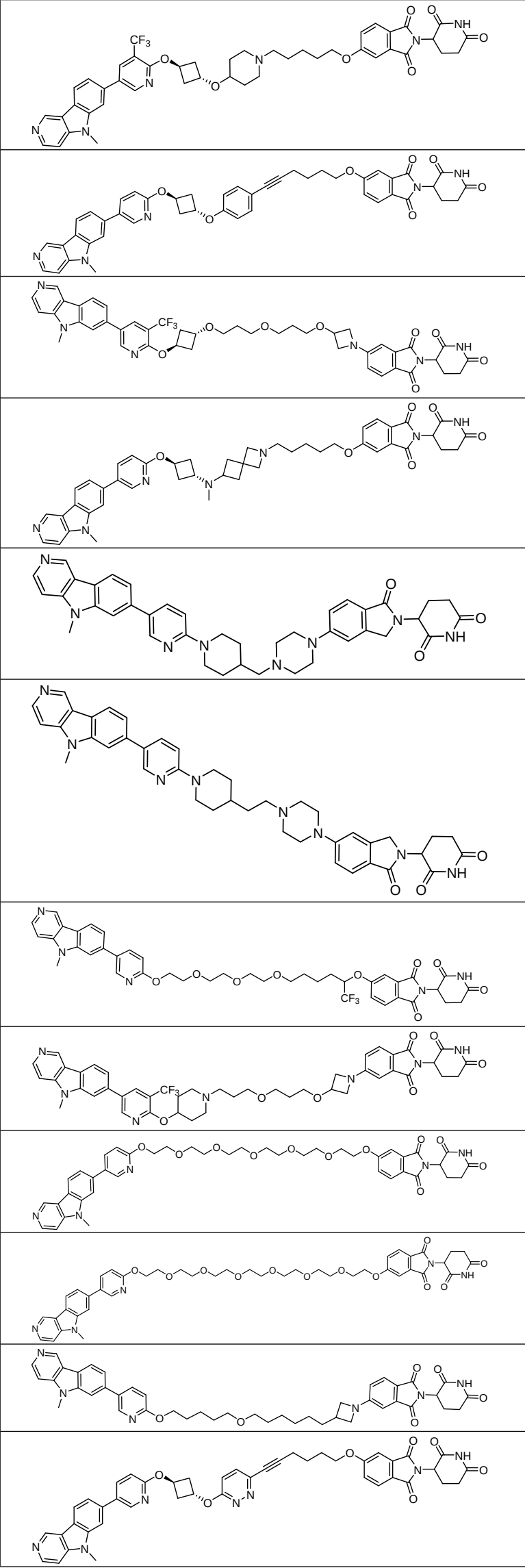
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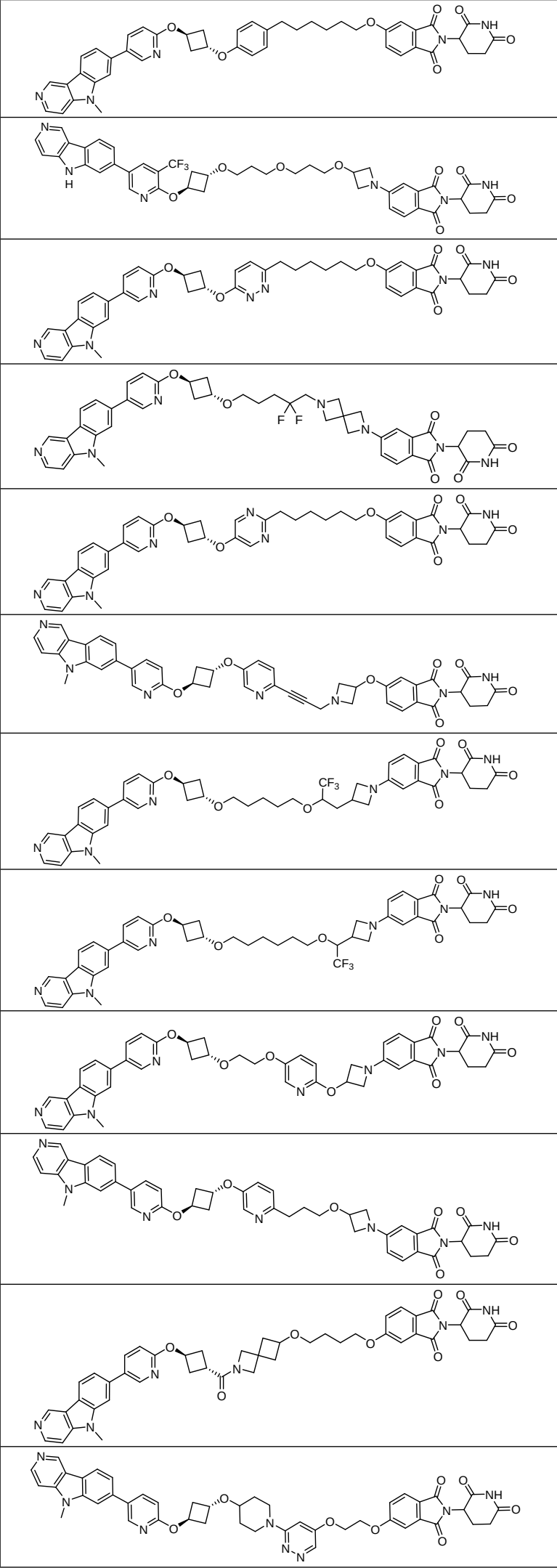




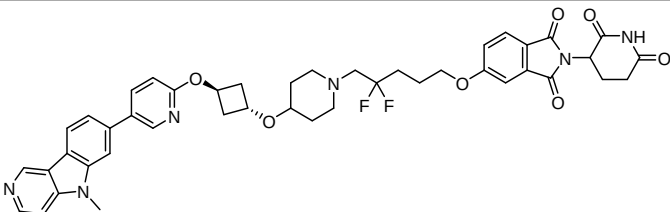
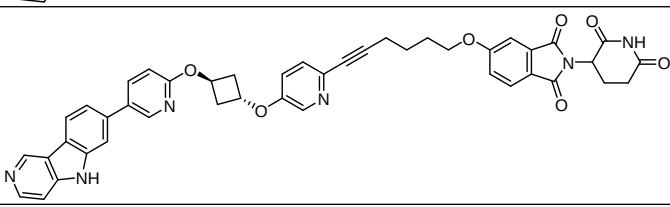
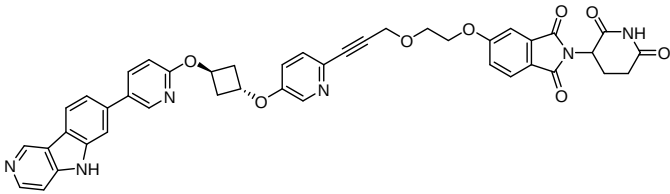
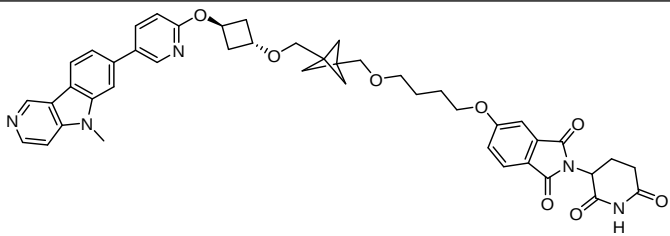
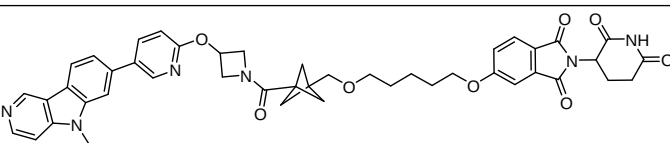
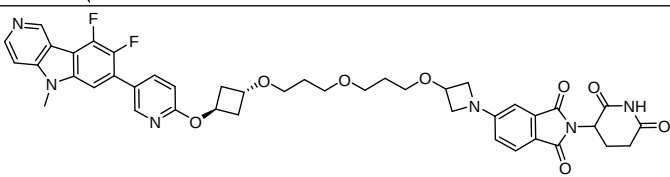
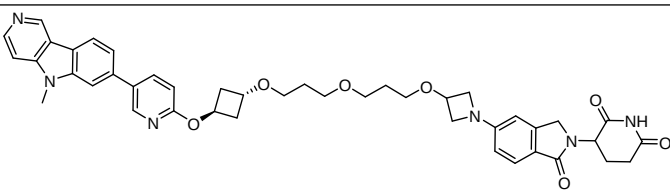
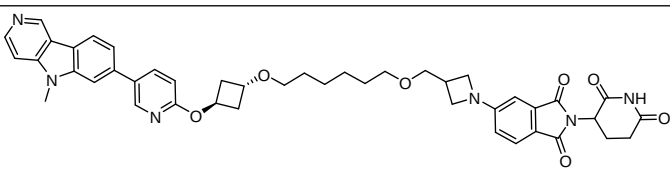
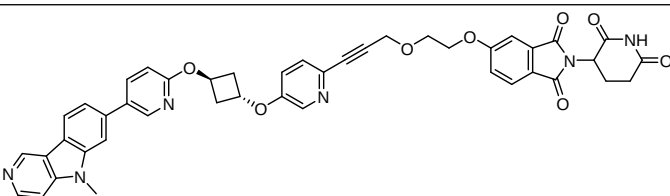
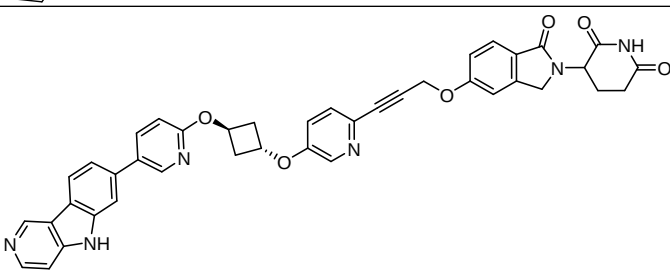
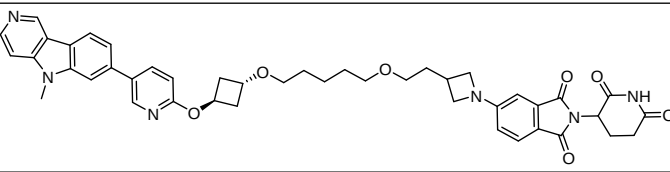
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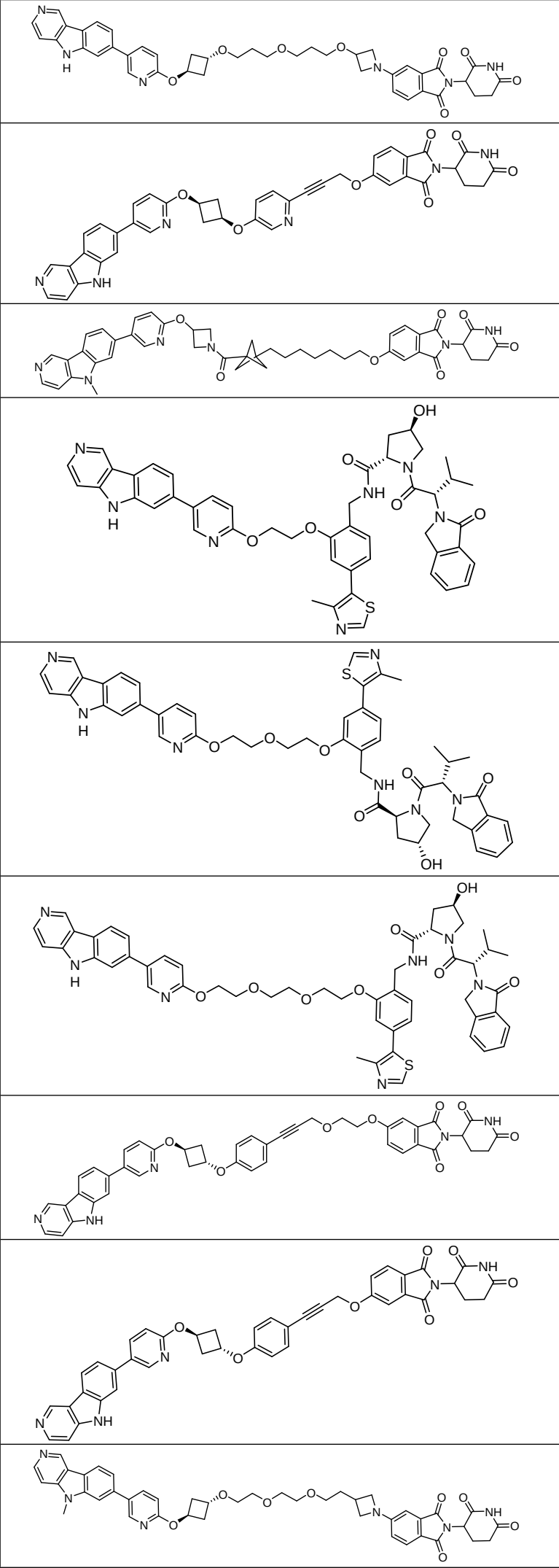




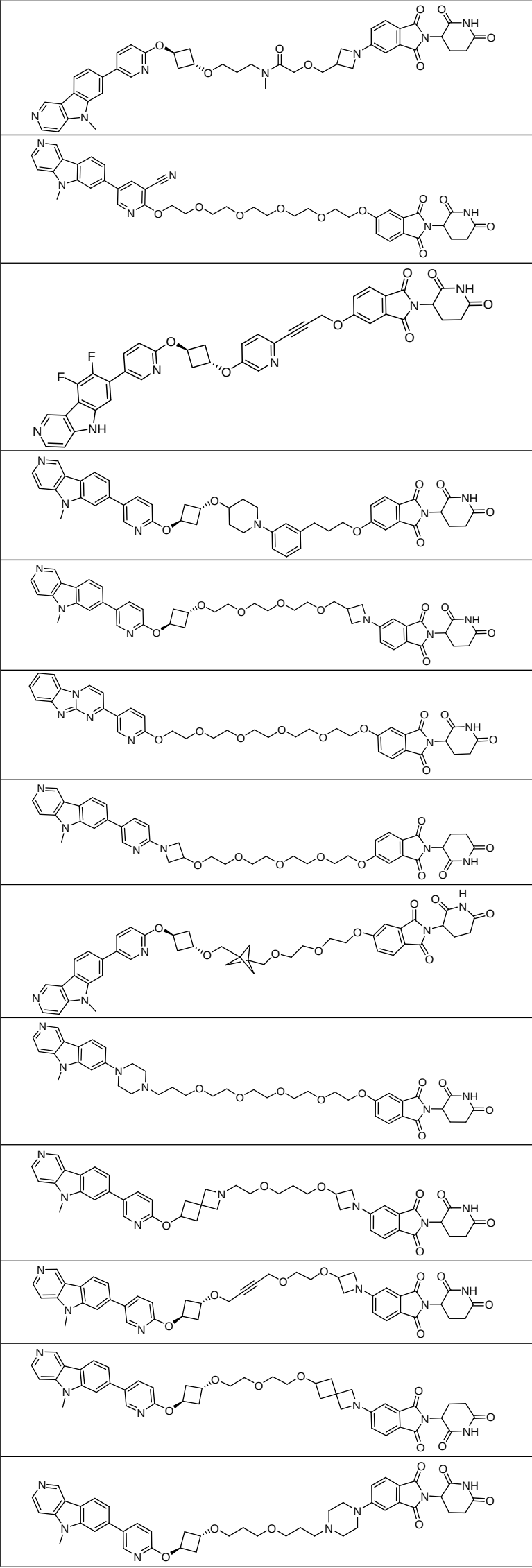


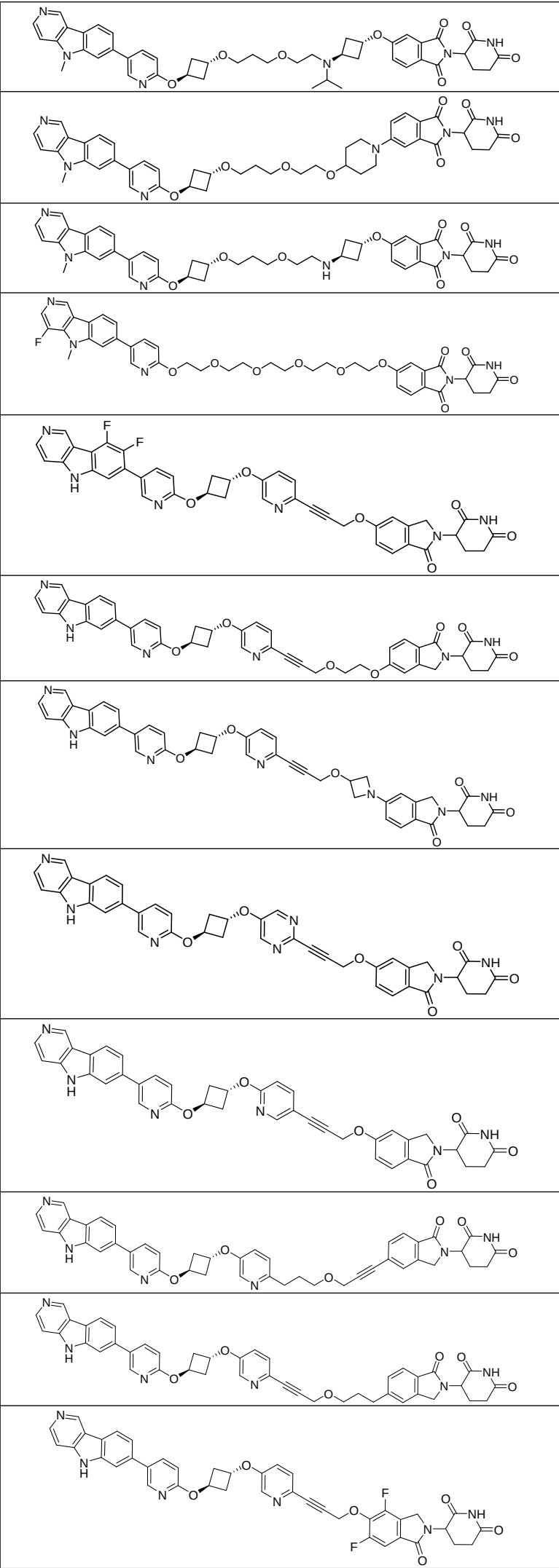


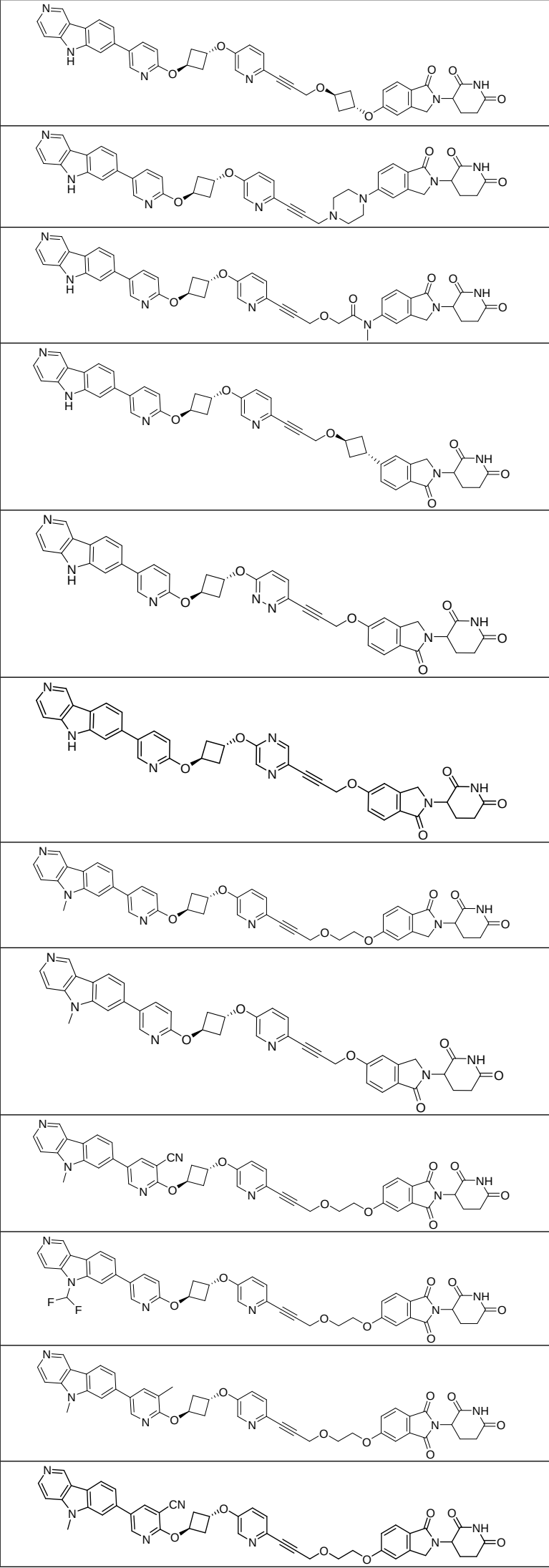
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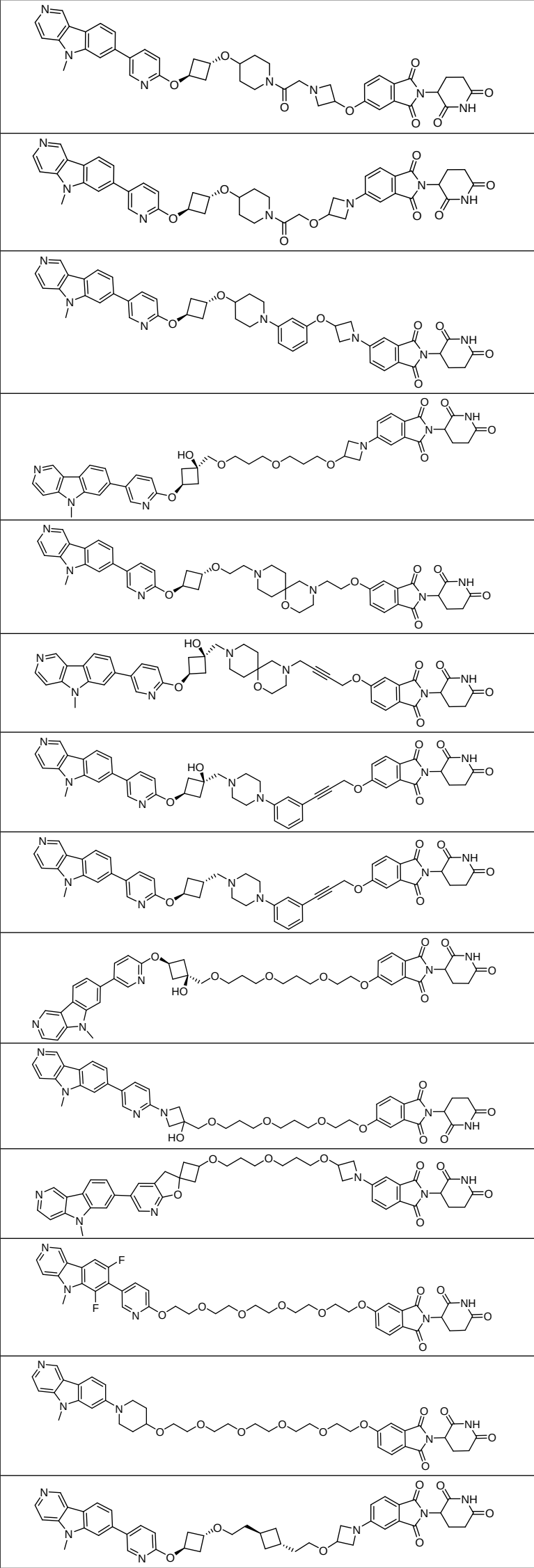


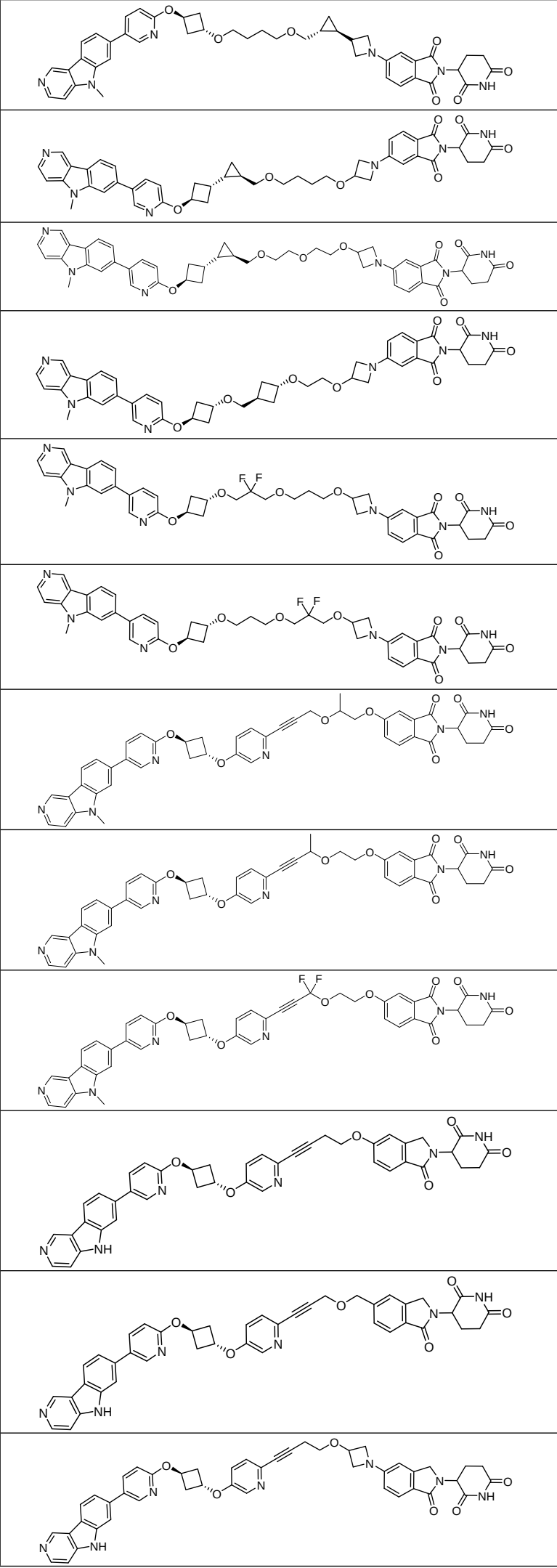


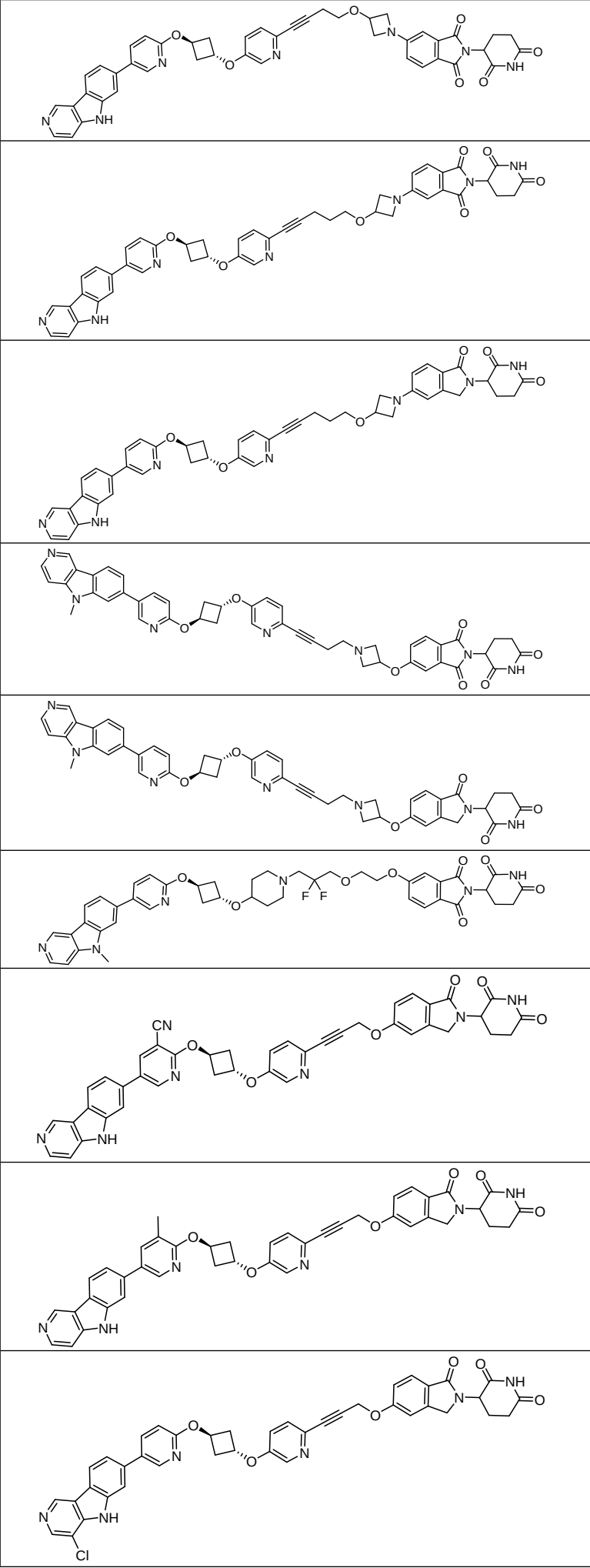


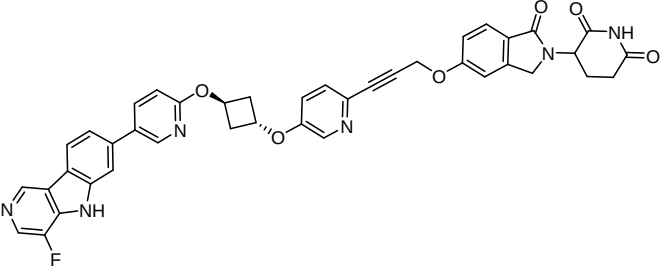
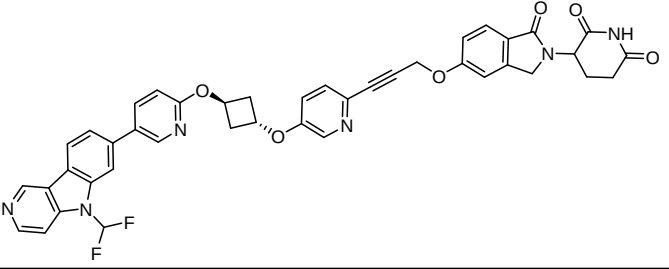
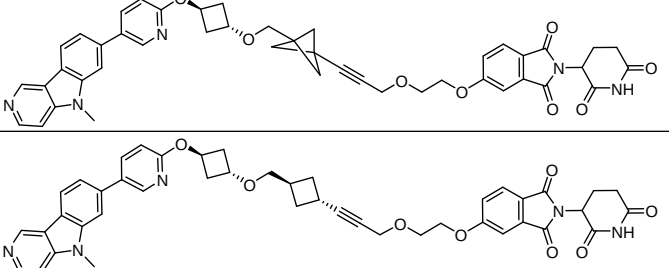
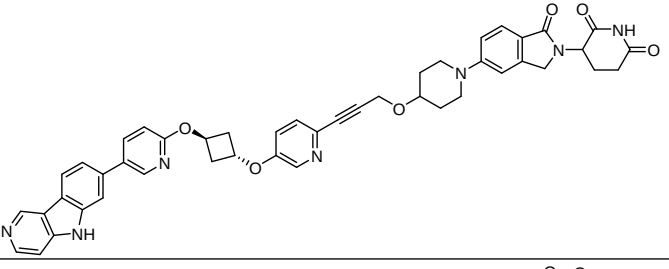
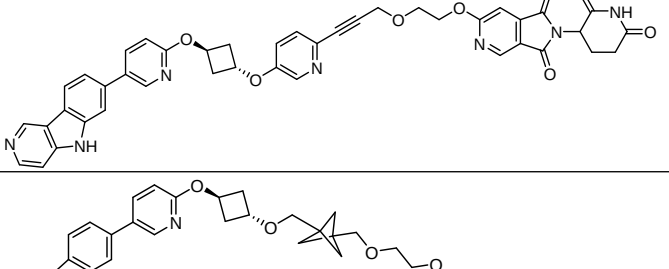
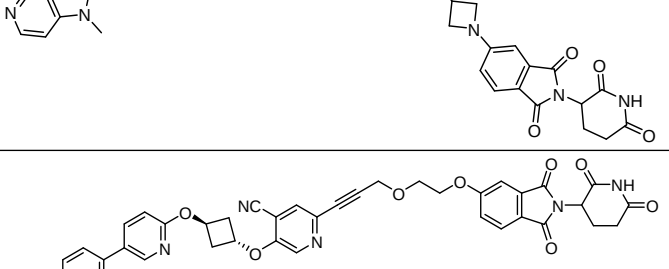
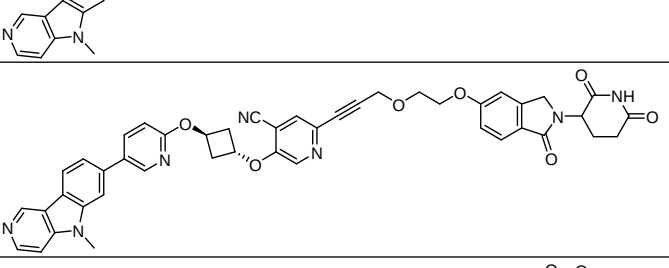
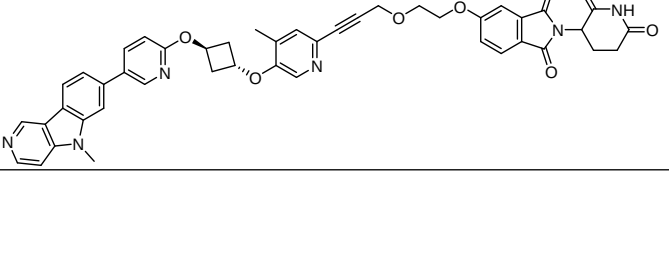


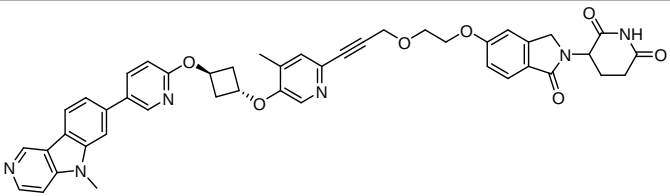
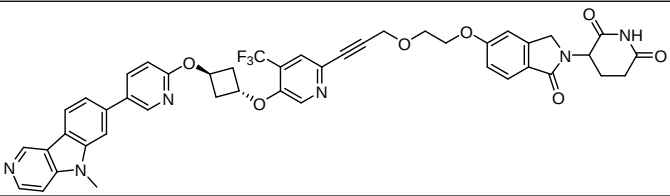
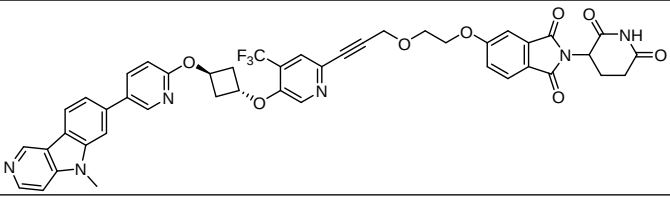
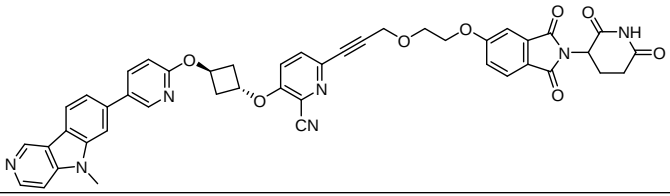
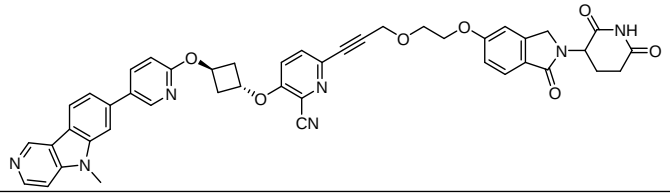
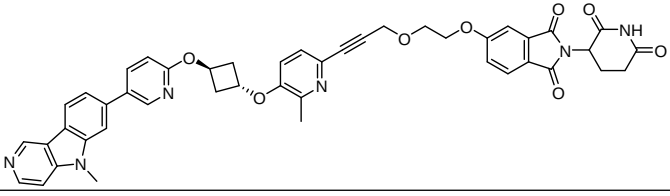
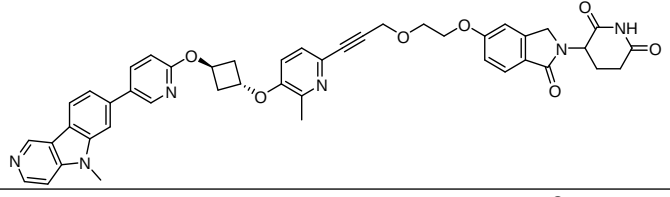
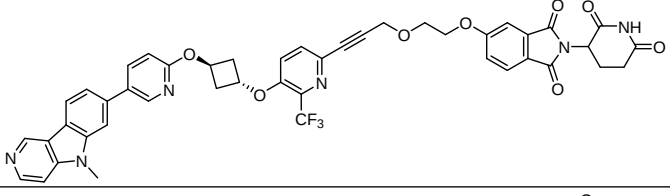
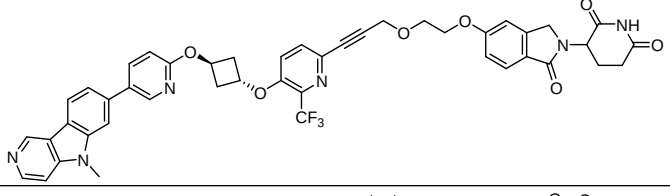
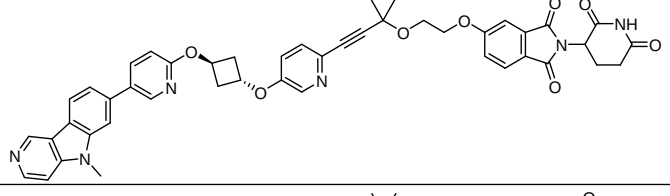
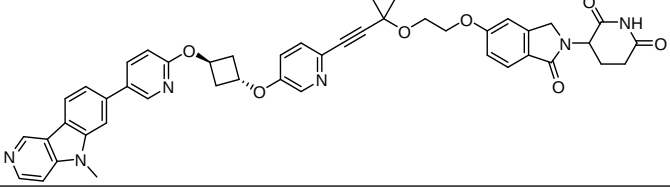


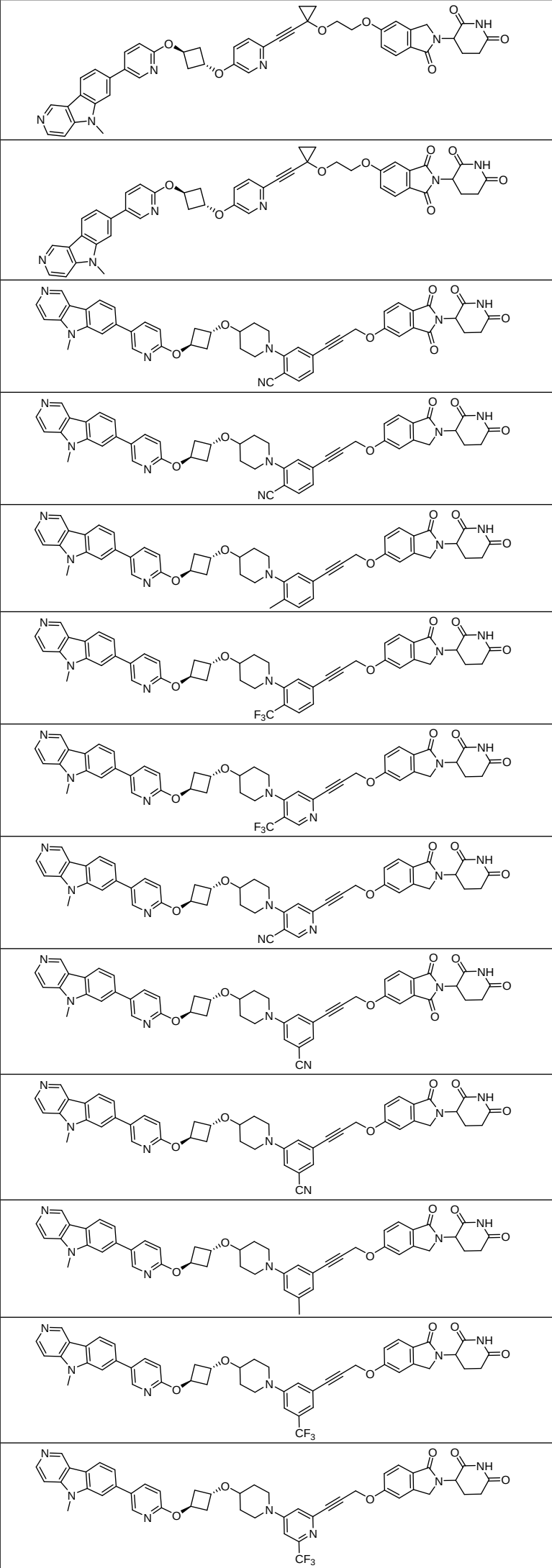




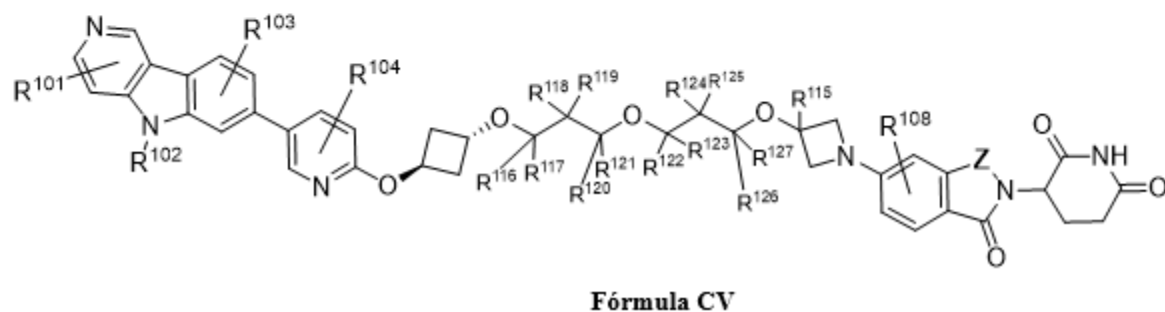
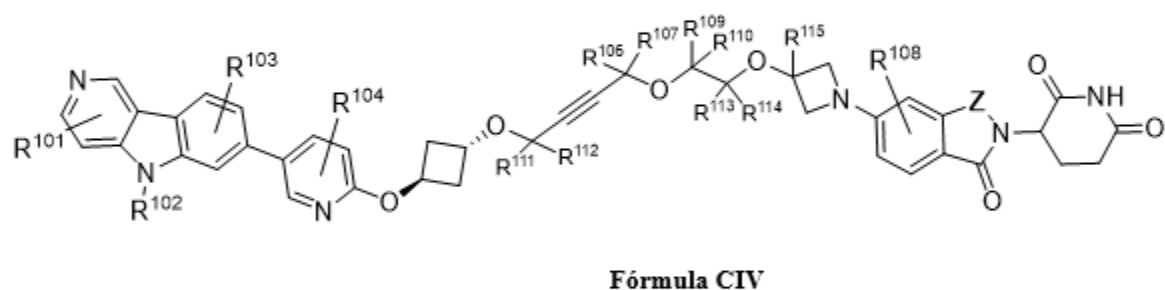
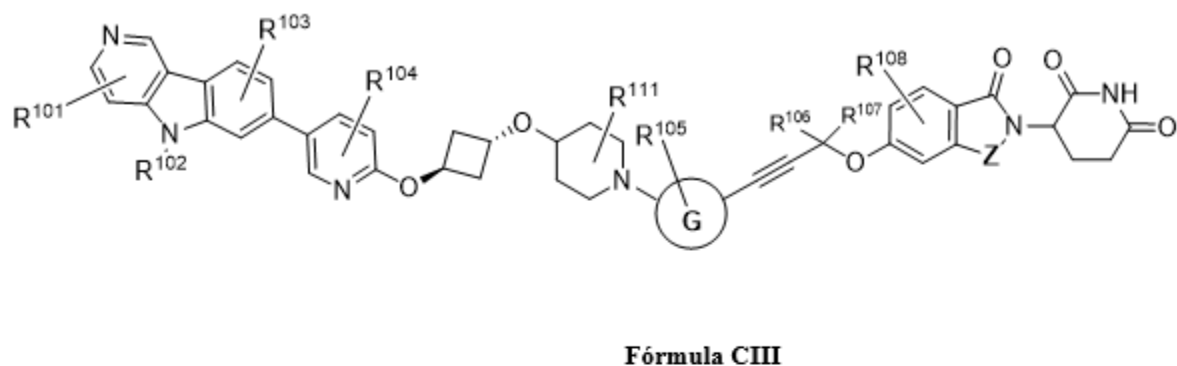
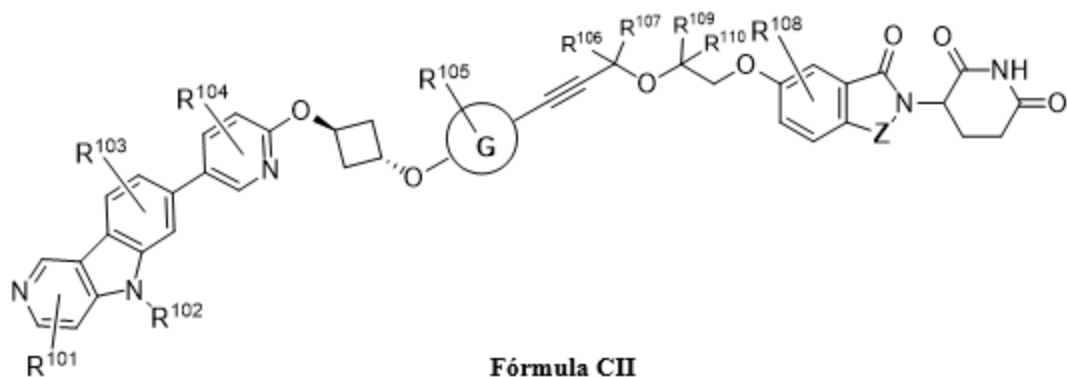


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en donde:

$R^{101}$  es 1–2 sustituyentes independientemente seleccionados de H, alquilo de  $C_{1-6}$ , halógeno, haloalquilo de  $C_{1-6}$ , y ciano;

$R^{102}$  se selecciona de H, alquilo de  $C_{1-6}$ , y haloalquilo de  $C_{1-6}$ ;

$R^{103}$  es 1–2 sustituyentes independientemente seleccionados de H, alquilo de  $C_{1-6}$ , halógeno, haloalquilo de  $C_{1-6}$ , y ciano;

$R^{104}$  es 1–2 sustituyentes independientemente seleccionados de H, alquilo de  $C_{1-6}$ , halógeno, haloalquilo de  $C_{1-6}$ , y ciano;

$R^{105}$  es 1–2 sustituyentes independientemente seleccionados de H, alquilo de  $C_{1-6}$ , halógeno, haloalquilo de  $C_{1-6}$ , y ciano;

$R^{106}$ ,  $R^{107}$ ,  $R^{109}$ ,  $R^{110}$ ,  $R^{111}$ ,  $R^{112}$ ,  $R^{113}$ ,  $R^{114}$ ,  $R^{116}$ ,  $R^{117}$ ,  $R^{120}$ ,  $R^{121}$ ,  $R^{126}$ ,  $R^{127}$ ,  $R^{122}$  y  $R^{123}$  son cada uno independientemente seleccionados de H, alquilo de  $C_{1-6}$ , halógeno, y haloalquilo de  $C_{1-6}$ ;

R<sup>108</sup> es 1–2 sustituyentes independientemente seleccionados de H, halógeno, ciano, y metoxi;

R<sup>115</sup> es H;

R<sup>118</sup> y R<sup>119</sup> son H o halógeno, o R<sup>118</sup> y R<sup>119</sup>, tomados juntos con el átomo de carbono al que se unen, forman C<sub>3-6</sub> cicloalquilo o heterociclilo de 3–6 miembros;

R<sup>124</sup> y R<sup>125</sup> son H o halógeno, o R<sup>124</sup> y R<sup>125</sup>, tomados juntos con el átomo de carbono al que se unen, forman C<sub>3-6</sub> cicloalquilo o heterociclilo de 3–6 miembros;

G es fenilo o heteroarilo de 5 o 6 miembros; y

Z es CH<sub>2</sub> o C=O.

14. Una composición farmacéutica que comprende un compuesto bifuncional de conformidad con alguna de las reivindicaciones 1 a 13, y un vehículo aceptable farmacéuticamente.
15. El compuesto de conformidad con alguna de las reivindicaciones 1 a 13, en donde R<sup>118</sup> y R<sup>119</sup>, tomados juntos con el átomo de carbono al que se unen, forman ciclopropanilo u oxetanilo.
16. El compuesto de conformidad con alguna de las reivindicaciones 1 a 13 y 15, en donde R<sup>124</sup> y R<sup>125</sup>, tomados juntos con el átomo de carbono al que se unen, forman ciclopropanilo u oxetanilo.