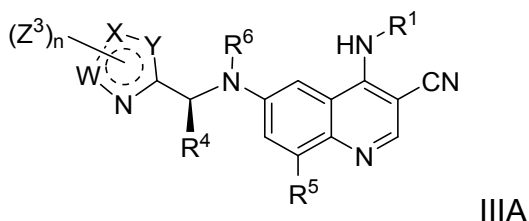


REIVINDICACIONES

1. Un compuesto que tiene la Formula IIIA:



en donde R¹ es hidrógeno, -O-R⁷, -N(R⁸)(R⁹), -C(O)-R⁷, -S(O)₂-R⁷, alquilo C₁-₉, alquenilo C₂-₆, alquinilo C₂-₆, cicloalquilo C₃-₁₅, heterociclilo, arilo, o heteroarilo;

en donde cada alquilo C₁-₉, alquenilo C₂-₆, alquinilo C₂-₆, cicloalquilo C₃-₁₅, heterociclilo, arilo, y heteroarilo puede estar sin sustituir o sustituido con uno a cuatro Z¹;

R⁴ es heterociclilo o heteroarilo, en donde cada heterociclilo o heteroarilo está sin sustituir o sustituido con uno a cuatro Z⁴;

R⁵ es hidrógeno, halo, -CN, -NO₂, -O-R⁷, -N(R⁸)(R⁹), -S(O)-R⁷, -S(O)₂R⁷, -S(O)₂N(R⁷)₂, -C(O)R⁷, -OC(O)-R⁷, -C(O)O-R⁷, -OC(O)O-R⁷, -OC(O)N(R¹⁰)(R¹¹), -C(O)N(R⁷)₂, -N(R⁷)C(O)(R⁷), alquilo C₁-₉, alquenilo C₂-₆, alquinilo C₂-₆, alquiltio C₁-₉, haloalquilo C₁-₆, cicloalquilo C₃-₁₅, arilo, heterociclilo, o heteroarilo;

en donde cada alquilo C₁-₉, alquenilo C₂-₆, alquinilo C₂-₆, alquiltio C₁-₉, haloalquilo C₁-₆, cicloalquilo C₃-₁₅, arilo, heterociclilo, y heteroarilo puede estar sin sustituir o sustituido con uno a cuatro Z⁵;

R⁶ es hidrógeno, -C(O)-R⁷, -C(O)O-R⁷, -C(O)N(R⁷)₂, alquilo C₁-₉, alquenilo C₂-₆, alquinilo C₂-₆, haloalquilo C₁-₆, cicloalquilo C₃-₁₅, arilo, heterociclilo, o heteroarilo;

en donde cada alquilo C₁-₉, alquenilo C₂-₆, alquinilo C₂-₆, haloalquilo C₁-₆, cicloalquilo C₃-₁₅, arilo, heterociclilo, y heteroarilo puede estar sin sustituir o sustituido con uno a cuatro Z⁶;

cada R⁷ es independientemente hidrógeno, alquilo C₁-₉, alquenilo C₂-₆, alquinilo C₂-₆, haloalquilo C₁-₆, cicloalquilo C₃-₁₅, arilo, heterociclilo, o heteroarilo;

en donde cada alquilo C₁-₉, alquenilo C₂-₆, alquinilo C₂-₆, haloalquilo C₁-₆, cicloalquilo C₃-₁₅, arilo, heterociclilo, y heteroarilo puede estar sin sustituir o sustituido con uno a cuatro Z⁷;

R⁸ y R⁹ en cada aparición son independientemente hidrógeno, -S(O)₂R¹⁰, -C(O)-R¹⁰, -C(O)O-R¹⁰, -C(O)N(R¹⁰)(R¹¹), alquilo C₁-₉, alquenilo C₂-₆, alquinilo C₂-₆, haloalquilo C₁-₆, cicloalquilo C₃-₁₅, arilo, heterociclilo, o heteroarilo;

en donde cada alquilo C₁-₉, alquenilo C₂-₆, alquinilo C₂-₆, haloalquilo C₁-₆, cicloalquilo C₃-₁₅, arilo, heterociclilo, o heteroarilo puede estar sin sustituir o sustituido con uno a cuatro Z⁸;

R^{10} y R^{11} en cada aparición son independientemente hidrógeno, alquilo C_{1-9} , alquenilo C_{2-6} , alquinilo C_{2-6} , haloalquilo C_{1-6} , cicloalquilo C_{3-15} , arilo, heterociclilo, o heteroarilo,

en donde cada alquilo C_{1-9} , alquenilo C_{2-6} , alquinilo C_{2-6} , haloalquilo C_{1-6} , cicloalquilo C_{3-15} , arilo, heterociclilo, y heteroarilo opcionalmente está sustituido con uno a cuatro Z^{1b} ;

Z^3, Z^4, Z^5, Z^6, Z^7 , y Z^8 es independientemente hidrógeno, oxo, halo, $-NO_2$, $-N_3$, $-CN$, tioxo, alquilo C_{1-9} , alquenilo C_{2-6} , alquinilo C_{2-6} , cicloalquilo C_{3-15} , haloalquilo C_{1-8} , arilo, heteroarilo, heterociclilo, $-O-R^{12}$, $-C(O)-R^{12}$, $-C(O)O-R^{12}$, $-C(O)-N(R^{13})(R^{14})$, $-N(R^{13})(R^{14})$, $-N(R^{13})_2(R^{14})^+$, $-N(R^{12})C(O)-R^{12}$, $-N(R^{12})C(O)O-R^{12}$, $-N(R^{12})C(O)N(R^{13})(R^{14})$, $-N(R^{12})S(O)_2(R^{12})$, $-NR^{12}S(O)_2N(R^{13})(R^{14})$, $-NR^{12}S(O)_2O(R^{12})$, $-OC(O)R^{12}$, $-OC(O)-N(R^{13})(R^{14})$, $-P(O)(OR^{12})_2$, $-OP(O)(OR^{12})_2$, $-CH_2P(O)(OR^{12})_2$, $-OCH_2P(O)(OR^{12})_2$, $-C(O)OCH_2P(O)(OR^{12})_2$, $-P(O)(R^{12})(OR^{12})$, $-OP(O)(R^{12})(OR^{12})$, $-CH_2P(O)(R^{12})(OR^{12})$, $-OCH_2P(O)(R^{12})(OR^{12})$, $-C(O)OCH_2P(O)(R^{12})(OR^{12})$, $-P(O)(N(R^{12})_2)_2$, $-OP(O)(N(R^{12})_2)_2$, $-CH_2P(O)(N(R^{12})_2)_2$, $-OCH_2P(O)(N(R^{12})_2)_2$, $-C(O)OCH_2P(O)(N(R^{12})_2)_2$, $-P(O)(N(R^{12})_2)(OR^{12})$, $-OP(O)(N(R^{12})_2)(OR^{12})$, $-CH_2P(O)(N(R^{12})_2)(OR^{12})$, $-OCH_2P(O)(N(R^{12})_2)(OR^{12})$, $-C(O)OCH_2P(O)(N(R^{12})_2)(OR^{12})$, $-P(O)(R^{12})(N(R^{12})_2)$, $-OP(O)(R^{12})(N(R^{12})_2)$, $-CH_2P(O)(R^{12})(N(R^{12})_2)$, $-OCH_2P(O)(R^{12})(N(R^{12})_2)$, $-C(O)OCH_2P(O)(R^{12})(N(R^{12})_2)$, $-Si(R^{12})_3$, $-S-R^{12}$, $-S(O)R^{12}$, $-S(O)(NH)R^{12}$, $-S(O)_2R^{12}$ o $-S(O)_2N(R^{13})(R^{14})$;

en donde cualquier alquilo, alquenilo, alquinilo, cicloalquilo, haloalquilo, arilo, heteroarilo o heterociclilo está sin sustituir o sustituido con uno a cuatro grupos Z^{1a} ;

cada Z^{1a} es independientemente oxo, halo, tioxo, $-NO_2$, $-CN$, $-N_3$, alquilo C_{1-9} , alquenilo C_{2-6} , alquinilo C_{2-6} , cicloalquilo C_{3-15} , haloalquilo C_{1-8} , arilo, heteroarilo, heterociclilo, $-O-R^{12}$, $-C(O)R^{12}$, $-C(O)O-R^{12}$, $-C(O)N(R^{13})(R^{14})$, $-N(R^{13})(R^{14})$, $-N(R^{13})_2(R^{14})^+$, $-N(R^{12})-C(O)R^{12}$, $-N(R^{12})C(O)O(R^{12})$, $-N(R^{12})C(O)N(R^{13})(R^{14})$, $-N(R^{12})S(O)_2(R^{12})$, $-N(R^{12})S(O)_2N(R^{13})(R^{14})$, $-N(R^{12})S(O)_2O(R^{12})$, $-OC(O)R^{12}$, $-OC(O)OR^{12}$, $-OC(O)-N(R^{13})(R^{14})$, $-Si(R^{12})_3$, $-S-R^{12}$, $-S(O)R^{12}$, $-S(O)(NH)R^{12}$, $-S(O)_2R^{12}$ o $-S(O)_2N(R^{13})(R^{14})$;

en donde cualquier alquilo, alquenilo, alquinilo, cicloalquilo, arilo, heteroarilo o heterociclilo está sin sustituir o sustituido con uno a cuatro grupos Z^{1b} ;

cada R^{12} es independientemente hidrógeno, alquilo C_{1-9} , alquenilo C_{2-6} , alquinilo C_{2-6} , cicloalquilo C_{3-15} , arilo, heteroarilo o heterociclilo,

en donde cualquier alquilo, alquenilo, alquinilo, cicloalquilo, arilo, heteroarilo o heterociclilo está sin sustituir o sustituido con uno a cuatro grupos Z^{1b} ;

R^{13} y R^{14} en cada aparición son cada uno independientemente hidrógeno, alquilo C_{1-9} , alquenilo C_{2-6} , alquinilo C_{2-6} , cicloalquilo C_{3-15} , arilo, heteroarilo o heterociclilo;

en donde cualquier alquilo, alquenilo, alquinilo, cicloalquilo, arilo, heteroarilo o heterociclilo está sin sustituir o sustituido con uno a cuatro grupos Z^{1b} , o R^{13} y R^{14} junto con el nitrógeno al que están unidos forman un heterociclilo, en donde dicho heterociclilo está sin sustituir o sustituido con uno a cuatro grupos Z^{1b} ;

cada R^{15} es independientemente halo, -CN, -NO₂, -O-R⁷, -N(R⁸)(R⁹), -S(O)-R⁷, -S(O)₂R⁷, -S(O)₂N(R⁷)₂, -C(O)R⁷, -OC(O)-R⁷, -C(O)O-R⁷, -OC(O)O-R⁷, -OC(O)N(R¹⁰)(R¹¹), -C(O)N(R⁷)₂, -N(R⁷)C(O)(R⁷), alquilo C_{1-9} , alquenilo C_{2-6} , alquinilo C_{2-6} , alquiltio C_{1-9} , haloalquilo C_{1-6} , cicloalquilo C_{3-15} , arilo, heterociclilo, o heteroarilo; y

cada Z^{1b} es independientemente oxo, tioxo, hidroxilo, halo, -NO₂, -N₃, -CN, alquilo C_{1-9} , alquenilo C_{2-6} , alquinilo C_{2-6} , cicloalquilo C_{3-15} , haloalquilo C_{1-8} , arilo, heteroarilo, heterociclilo, -O(alquilo C_{1-9}), -O(alquenilo C_{2-6}), -O(alquinilo C_{2-6}), -O(cicloalquilo C_{3-15}), -O(haloalquilo C_{1-8}), -O(arilo), -O(heteroarilo), -O(heterociclilo), -NH₂, -NH(alquilo C_{1-9}), -NH(alquenilo C_{2-6}), -NH(alquinilo C_{2-6}), -NH(cicloalquilo C_{3-15}), -NH(haloalquilo C_{1-8}), -NH(arilo), -NH(heteroarilo), -NH(heterociclilo), -N(alquilo C_{1-9})₂, -N(alquenilo C_{2-6})₂, -N(alquinilo C_{2-6})₂, -N(cicloalquilo C_{3-15})₂, -N(haloalquilo C_{1-8})₂, -N(arilo)₂, -N(heteroarilo)₂, -N(heterociclilo)₂, -N(alquilo C_{1-9})(alquenilo C_{2-6}), -N(alquilo C_{1-9})(alquinilo C_{2-6}), -N(alquilo C_{1-9})(cicloalquilo C_{3-15}), -N(alquilo C_{1-9})(haloalquilo C_{1-8}), -N(alquilo C_{1-9})(arilo), -N(alquilo C_{1-9})(heteroarilo), -N(alquilo C_{1-9})(heterociclilo), -C(O)(alquilo C_{1-9}), -C(O)(alquenilo C_{2-6}), -C(O)(alquinilo C_{2-6}), -C(O)(cicloalquilo C_{3-15}), -C(O)(haloalquilo C_{1-8}), -C(O)(arilo), -C(O)(heteroarilo), -C(O)(heterociclilo), -C(O)O(alquilo C_{1-9}), -C(O)O(alquenilo C_{2-6}), -C(O)O(alquinilo C_{2-6}), -C(O)O(cicloalquilo C_{3-15}), -C(O)O(haloalquilo C_{1-8}), -C(O)O(arilo), -C(O)O(heteroarilo), -C(O)O(heterociclilo), -C(O)NH₂, -C(O)NH(alquilo C_{1-9}), -C(O)NH(alquenilo C_{2-6}), -C(O)NH(alquinilo C_{2-6}), -C(O)NH(cicloalquilo C_{3-15}), -C(O)NH(haloalquilo C_{1-8}), -C(O)NH(arilo), -C(O)NH(heteroarilo), -C(O)NH(heterociclilo), -C(O)N(alquilo C_{1-9})₂, -C(O)N(alquenilo C_{2-6})₂, -C(O)N(alquinilo C_{2-6})₂, -C(O)N(cicloalquilo C_{3-15})₂, -C(O)N(haloalquilo C_{1-8})₂, -C(O)N(arilo)₂, -C(O)N(heteroarilo)₂, -C(O)N(heterociclilo)₂, -NHC(O)(alquilo C_{1-9}), -NHC(O)(alquenilo C_{2-6}), -NHC(O)(alquinilo C_{2-6}), -NHC(O)(cicloalquilo C_{3-15}), -NHC(O)(haloalquilo C_{1-8}), -NHC(O)(arilo), -NHC(O)(heteroarilo), -NHC(O)(heterociclilo), -NHC(O)O(alquilo C_{1-9}), -NHC(O)O(alquenilo C_{2-6}), -NHC(O)O(alquinilo C_{2-6}), -NHC(O)O(cicloalquilo C_{3-15}), -NHC(O)O(haloalquilo C_{1-8}), -NHC(O)O(arilo), -NHC(O)O(heteroarilo), -NHC(O)O(heterociclilo), -NHC(O)NH(alquilo C_{1-9}), -NHC(O)NH(alquenilo C_{2-6}), -NHC(O)NH(alquinilo C_{2-6}).

₆), -NHC(O)NH(cicloalquilo C₃₋₁₅), -NHC(O)NH(haloalquilo C₁₋₈), -NHC(O)NH(arilo), -NHC(O)NH(heteroarilo), -NHC(O)NH(heterociclilo), -SH, -S(alquilo C₁₋₉), -S(alquenilo C₂₋₆), -S(alquinilo C₂₋₆), -S(cicloalquilo C₃₋₁₅), -S(haloalquilo C₁₋₈), -S(arilo), -S(heteroarilo), -S(heterociclilo), -NHS(O)(alquilo C₁₋₉), -N(alquilo C₁₋₉)S(O)(alquilo C₁₋₉), -S(O)N(alquilo C₁₋₉)₂, -S(O)(alquilo C₁₋₉), -S(O)(NH)(alquilo C₁₋₉), -S(O)(alquenilo C₂₋₆), -S(O)(alquinilo C₂₋₆), -S(O)(cicloalquilo C₃₋₁₅), -S(O)(haloalquilo C₁₋₈), -S(O)(arilo), -S(O)(heteroarilo), -S(O)(heterociclilo), -S(O)₂(alquilo C₁₋₉), -S(O)₂(alquenilo C₂₋₆), -S(O)₂(alquinilo C₂₋₆), -S(O)₂(cicloalquilo C₃₋₁₅), -S(O)₂(haloalquilo C₁₋₈), -S(O)₂(arilo), -S(O)₂(heteroarilo), -S(O)₂(heterociclilo), -S(O)₂NH(alquilo C₁₋₉), o -S(O)₂N(alquilo C₁₋₉)₂;

en donde cualquier alquilo, cicloalquilo, arilo, heteroarilo, o heterociclilo está sin sustituir o sustituido con uno a cuatro halo, alquilo C₁₋₉, haloalquilo C₁₋₈, -OH, -NH₂, -NH(alquilo C₁₋₉), -NH(cicloalquilo C₃₋₁₅), -NH(haloalquilo C₁₋₈), -NH(arilo), -NH(heteroarilo), -NH(heterociclilo), -N(alquilo C₁₋₉)₂, -N(cicloalquilo C₃₋₁₅)₂, -NHC(O)(cicloalquilo C₃₋₁₅), -NHC(O)(haloalquilo C₁₋₈), -NHC(O)(arilo), -NHC(O)(heteroarilo), -NHC(O)(heterociclilo), -NHC(O)O(alquilo C₁₋₉), -NHC(O)O(alquinilo C₂₋₆), -NHC(O)O(cicloalquilo C₃₋₁₅), -NHC(O)O(haloalquilo C₁₋₈), -NHC(O)O(arilo), -NHC(O)O(heteroarilo), -NHC(O)O(heterociclilo), -NHC(O)NH(alquilo C₁₋₉), -S(O)(NH)(alquilo C₁₋₉), S(O)₂(alquilo C₁₋₉), -S(O)₂(cicloalquilo C₃₋₁₅), -S(O)₂(haloalquilo C₁₋₈), -S(O)₂(arilo), -S(O)₂(heteroarilo), -S(O)₂(heterociclilo), -S(O)₂NH(alquilo C₁₋₉), -S(O)₂N(alquilo C₁₋₉)₂, -O(cicloalquilo C₃₋₁₅), -O(haloalquilo C₁₋₈), -O(arilo), -O(heteroarilo), -O(heterociclilo), o -O(alquilo C₁₋₉);

W, X y Y son cada uno independientemente N o C; y
n es 1, 2, o 3;

o una sal, estereoisómero, mezcla de estereoisómeros, o análogo deuterado farmacéuticamente aceptable del mismo.

2. El compuesto de la reivindicación 1, en donde

- (i) R⁵ es hidrógeno, halo, -CN, O-R⁷, -S(O)-R⁷, -S(O)₂R⁷, -S(O)₂N(R⁷)₂, -C(O)R⁷, -C(O)N(R⁷)₂, alquilo C₁₋₉, alquenilo C₂₋₆, alquinilo C₂₋₆, cicloalquilo C₃₋₁₅, arilo, heterociclilo, o heteroarilo;

en donde cada alquilo C₁₋₉, alquenilo C₂₋₆, alquinilo C₂₋₆, cicloalquilo C₃₋₁₅, arilo, heterociclilo, y heteroarilo puede estar sin sustituir o sustituido con uno a cuatro Z⁵, o una sal farmacéuticamente aceptable del mismo, o

R⁵ es hidrógeno, halo, -CN, -C(O)R⁷, -O-R⁷, -S(O)₂R⁷ o heteroarilo, o una sal farmacéuticamente aceptable del mismo; y/o

- (ii) R⁶ es hidrógeno, o una sal farmacéuticamente aceptable del mismo; y/o
- (iii) R¹ es -O-R⁷, alquilo C₁₋₉, cicloalquilo C₃₋₁₅, heterociclilo, arilo, o heteroarilo; y dicho alquilo C₁₋₉, cicloalquilo C₃₋₁₅, heterociclilo, arilo, o heteroarilo puede estar sin sustituir o sustituido con uno a cuatro sustituyentes seleccionados independientemente del grupo que consiste en halo, -CN, -O-R¹², -S(O)₂R¹², alquilo C₁₋₉, haloalquilo C₁₋₉, cicloalquilo C₃₋₁₅, heterociclilo, y arilo, en donde dicho cicloalquilo C₃₋₁₅ puede estar sin sustituir o sustituido con uno a cuatro sustituyentes seleccionados independientemente del grupo que consiste en alquilo C₁₋₉, y haloalquilo C₁₋₉, o una sal farmacéuticamente aceptable del mismo, o

R¹ es alquilo C₁₋₉, sin sustituir o sustituido con uno a tres sustituyentes seleccionados independientemente del grupo que consiste en halo, -CN, -O-R¹², -S(O)₂R¹², cicloalquilo C₃₋₁₅, heterociclilo, y arilo, en donde dicho cicloalquilo C₃₋₁₅ o heterociclilo puede estar sin sustituir o sustituido con uno a cuatro sustituyentes seleccionados independientemente del grupo que consiste en alquilo C₁₋₉, y haloalquilo C₁₋₉, o una sal farmacéuticamente aceptable del mismo, o

R¹ es cicloalquilo C₃₋₁₅, heterociclilo, o heteroarilo, en donde dicho cicloalquilo C₃₋₁₅, heterociclilo, o heteroarilo está sin sustituir o sustituido con uno a tres sustituyentes seleccionados independientemente del grupo que consiste en halo, -CN, -O-R¹², alquilo C₁₋₉, y arilo, o una sal farmacéuticamente aceptable del mismo, o

R¹ es heterociclilo o heteroarilo, en donde dicho heterociclilo o heteroarilo está sin sustituir o sustituido con uno a tres sustituyentes seleccionados independientemente del grupo que consiste en halo, y alquilo C₁₋₉, o una sal farmacéuticamente aceptable del mismo, o

R¹ es arilo, sin sustituir o sustituido con uno a tres sustituyentes seleccionados independientemente del grupo que consiste en halo, -CN, -O-R⁷, alquilo C₁₋₉, y arilo, o una sal farmacéuticamente aceptable del mismo, o

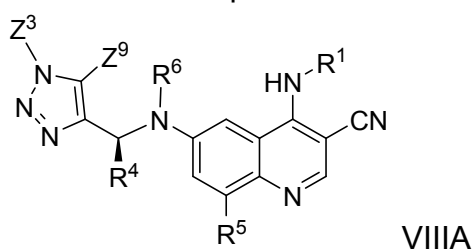
R^1 es arilo, sin sustituir o sustituido con uno a tres sustituyentes seleccionados independientemente del grupo que consiste en halo, -O- R^7 , y alquilo C_{1-9} , o una sal farmacéuticamente aceptable del mismo.

3. El compuesto de la reivindicación 1, en donde

- (1) W es N, X es N- Z^3 , y Y es C- Z^3 , o una sal farmacéuticamente aceptable del mismo; y/o
- (2) Z^3 es hidrógeno o alquilo C_{1-9} sin sustituir o sustituido con uno a cuatro sustituyentes seleccionados independientemente del grupo que consiste en -CN, halo, -O- R^{12} , -C(O)O- R^{12} , -OC(O)- R^{12} , -N(R^{13})(R^{14}), -N(R^{13})₂(R^{14})⁺, -C(O)N(R^{12})-S(O)₂ R^{12} , alquilo C_{1-9} , heterociclilo, arilo, y heteroarilo, o una sal farmacéuticamente aceptable del mismo, o

Z^3 es cicloalquilo C_{3-15} , heterociclilo, arilo, o heteroarilo; y dicho cicloalquilo C_{3-15} , heterociclilo, arilo, o heteroarilo, puede estar sin sustituir o sustituido con uno a cuatro sustituyentes seleccionados independientemente del grupo que consiste en -CN, halo, -O- R^{12} , -C(O)- R^{12} , -C(O)O- R^{12} , -OC(O)- R^{12} , -N(R^{13})(R^{14}), -N(R^{13})₂(R^{14})⁺, alquilo C_{1-9} , haloalquilo C_{1-8} , hidroxialquilo C_{1-8} , cicloalquilo C_{3-15} , heterociclilo, y heteroarilo, o una sal farmacéuticamente aceptable del mismo.

4. El compuesto de la reivindicación 1 que tiene la Formula VIIIA:



en donde Z^3 , R^1 , R^4 , R^5 y R^6 son como se definen en la reivindicación 1, y Z^9 es hidrógeno, halo, -CN, o -O- R^{12} ; o una sal, estereoisómero, mezcla de estereoisómeros, o análogo deuterado farmacéuticamente aceptable del mismo.

5. El compuesto de la reivindicación 4, en donde:

Z^3 es hidrógeno, alquilo C_{1-9} , cicloalquilo C_{3-15} , heterociclilo, arilo, o heteroarilo; en donde dicho alquilo C_{1-9} , cicloalquilo C_{3-15} , o heterociclilo puede estar sin sustituir o sustituido con uno a cuatro sustituyentes seleccionados independientemente del grupo que consiste en oxo, -CN, halo, -O- R^{12} , -C(O)- R^{12} , -C(O)O- R^{12} , -OC(O)- R^{12} , -C(O)-N(R^{13})(R^{14}), -N(R^{12})S(O)₂(R^{12}), -N(R^{13})(R^{14}),

$-N(R^{13})_2(R^{14})^+$, $-C(O)N(R^{12})-S(O)_2R^{12}$, alquilo C_{1-9} , haloalquilo C_{1-8} , hidroxialquilo C_{1-8} , cicloalquilo C_{3-15} , arilo, heterociclilo, y heteroarilo;

Z^9 es hidrógeno;

R^1 es alquilo C_{1-9} , cicloalquilo C_{3-15} , heterociclilo, arilo, o heteroarilo;
 en donde dicho alquilo C_{1-9} , heterociclilo, arilo, o heteroarilo puede estar sin sustituir o sustituido con uno a tres sustituyentes seleccionados independientemente del grupo que consiste en halo, $-CN$, $-O-R^{12}$, $-S(O)_2R^{12}$, alquilo C_{1-9} , haloalquilo C_{1-9} , heterociclilo, y arilo, en donde dicho C_{3-15} cicloalquilo puede estar sin sustituir o sustituido con uno a cuatro sustituyentes seleccionados independientemente del grupo que consiste en alquilo C_{1-9} , y haloalquilo C_{1-9} ;

R^4 es heterociclilo o heteroarilo;
 en donde dicho heterociclilo o heteroarilo está sin sustituir o sustituido con uno a tres sustituyentes seleccionados independientemente del grupo que consiste en $-CN$, halo, $-O-R^{12}$, $-C(O)-R^{12}$, $-N(R^{13})(R^{14})$, alquilo C_{1-9} , haloalquilo C_{1-9} , y heterociclilo;

R^5 es $-CN$, halo, $-O-R^7$ o $-S(O)_2R^7$;

R^6 es hidrógeno;

cada R^7 es independientemente hidrógeno o alquilo C_{1-9} ;
 en donde dicho alquilo C_{1-9} puede estar sin sustituir o sustituido con uno a tres sustituyentes seleccionados independientemente del grupo que consiste en hidroxilo, halo, $-O(\text{alquilo } C_{1-9})$ y arilo;

cada R^{12} es independientemente hidrógeno, alquilo C_{1-9} o heterociclilo;
 en donde dicho alquilo C_{1-9} puede estar sin sustituir o sustituido con uno a tres sustituyentes seleccionados independientemente del grupo que consiste en hidroxilo, halo, $-O(\text{alquilo } C_{1-9})$ y arilo; y

cada R^{13} y R^{14} es independientemente hidrógeno o alquilo C_{1-9} ;
 en donde dicho alquilo C_{1-9} puede estar sin sustituir o sustituido con uno a tres sustituyentes seleccionados independientemente del grupo que consiste en hidroxilo, halo, $-O(\text{alquilo } C_{1-9})$ y arilo;

o una sal, estereoisómero, mezcla de estereoisómeros farmacéuticamente aceptable del mismo.

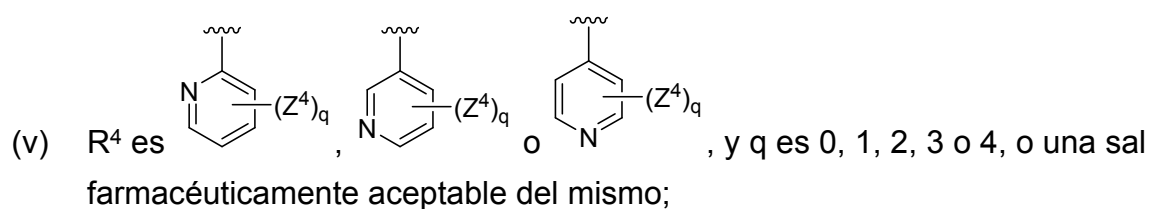
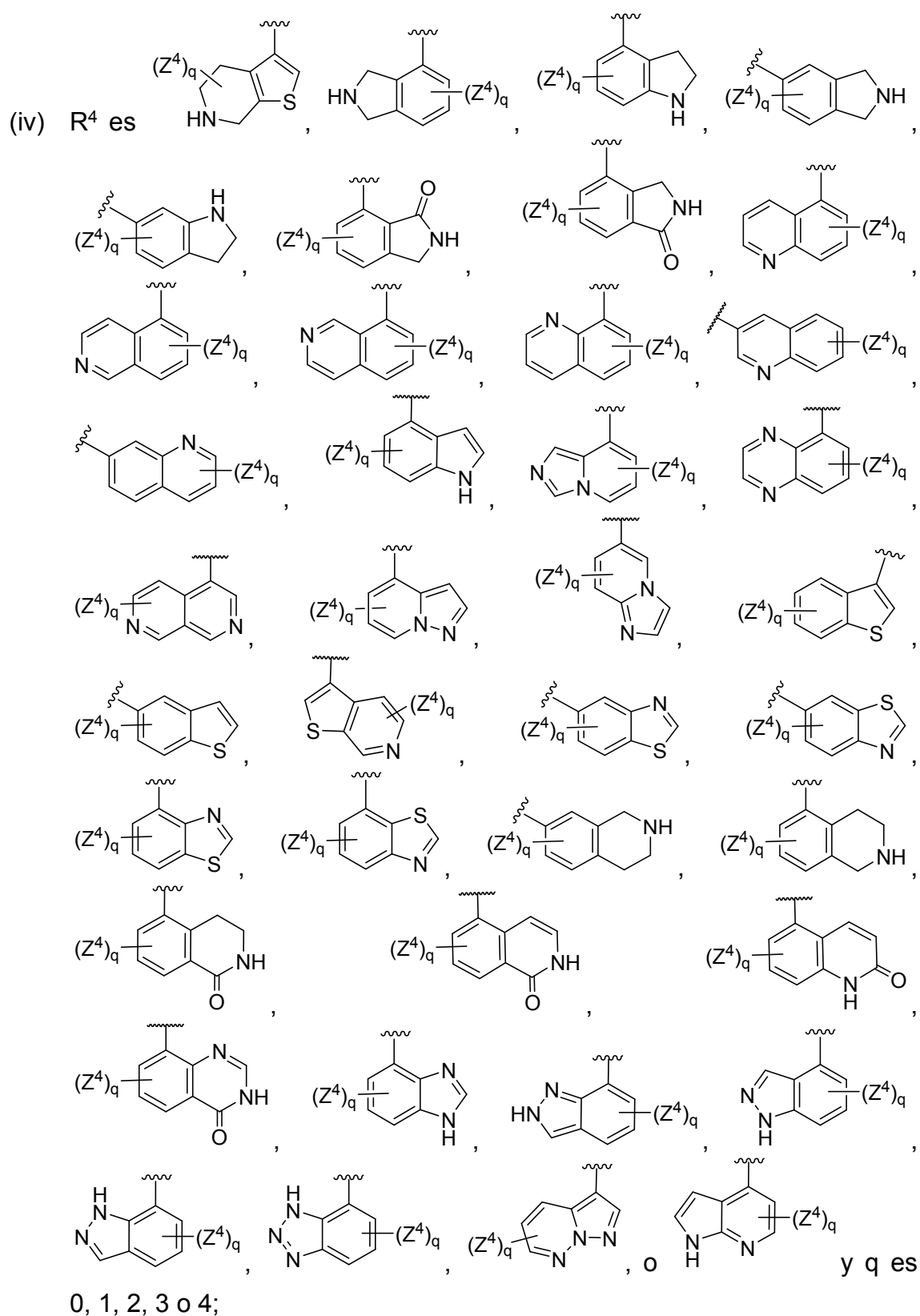
6. El compuesto de la reivindicación 5, en donde Z^3 es cicloalquilo C_{3-15} sin sustituir o sustituido con uno a cuatro sustituyentes seleccionados independientemente del grupo que consiste en $-CN$, halo, $-C(O)-R^{12}$, $-OC(O)-R^{12}$, $-C(O)N(R^{13})(R^{14})$, alquilo C_{1-9} , haloalquilo C_{1-8} , hidroxialquilo C_{1-8} , cicloalquilo C_{3-15} , y heteroarilo, o una sal farmacéuticamente aceptable del mismo, o

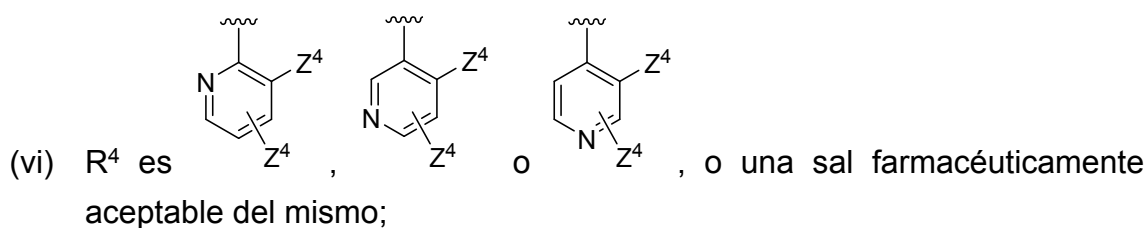
Z^3 es heterociclilo sin sustituir o sustituido con uno a cuatro sustituyentes seleccionados independientemente del grupo que consiste en $-O-R^{12}$, $-C(O)O-R^{12}$, alquilo C_{1-9} , haloalquilo C_{1-8} , hidroxialquilo C_{1-8} , y heterociclilo, o una sal farmacéuticamente aceptable del mismo.

7. El compuesto de la reivindicación 4 o 5, en donde R^5 es ciano o halo, o una sal farmacéuticamente aceptable del mismo; o R^6 es hidrógeno, o una sal farmacéuticamente aceptable del mismo.

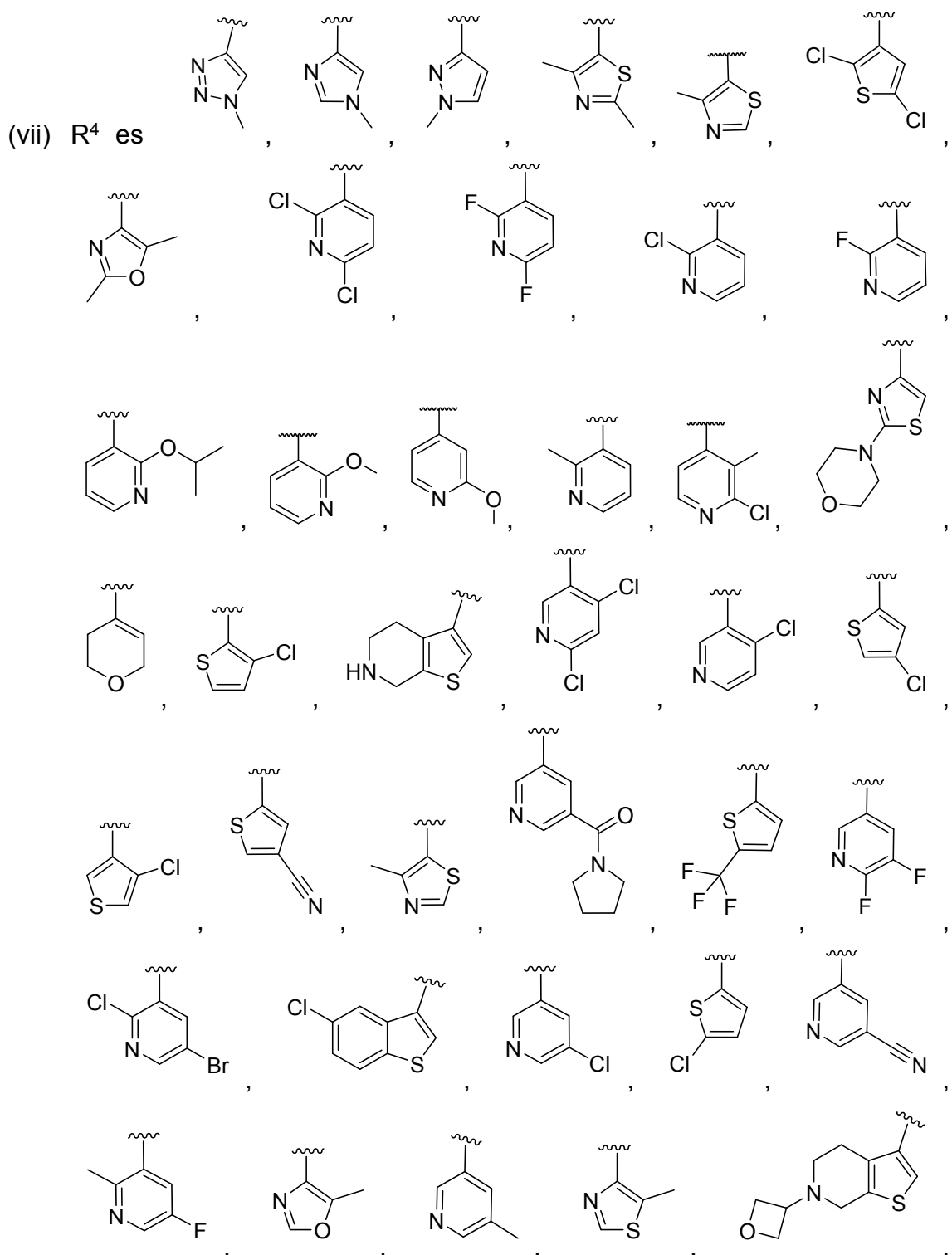
8. El compuesto de la reivindicación 1, en donde

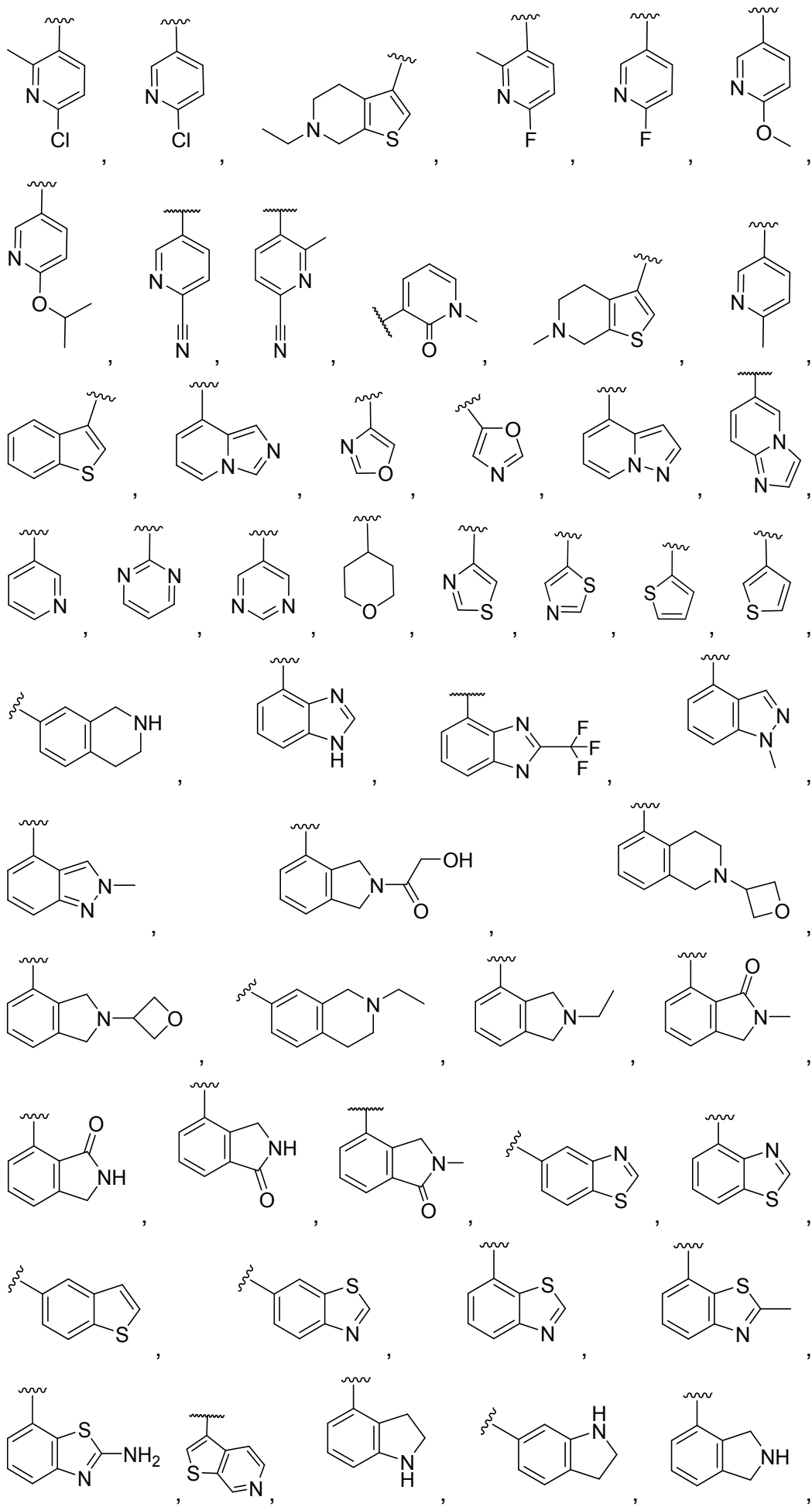
- (i) R^4 es heterociclilo o heteroarilo; y dicho heterociclilo o heteroarilo está sin sustituir o sustituido con uno a tres sustituyentes seleccionados independientemente del grupo que consiste en $-CN$, halo, $-O-R^{12}$, $-C(O)-R^{12}$, $-N(R^{13})(R^{14})$, alquilo C_{1-9} , haloalquilo C_{1-9} , y heterociclilo, o una sal farmacéuticamente aceptable del mismo;
- (ii) R^4 es heteroarilo sin sustituir o sustituido con uno a tres sustituyentes seleccionados independientemente del grupo que consiste en $-CN$, halo, $-O-R^{12}$, $-C(O)-R^{12}$, $-N(R^{13})(R^{14})$, alquilo C_{1-9} , haloalquilo C_{1-9} , y heterociclilo, o una sal farmacéuticamente aceptable del mismo;
- (iii) R^4 es heterociclilo sin sustituir o sustituido con uno a tres sustituyentes seleccionados independientemente del grupo que consiste en $-CN$, halo, $-O-R^{12}$, $-C(O)-R^{12}$, $-N(R^{13})(R^{14})$, alquilo C_{1-9} , haloalquilo C_{1-9} , y heterociclilo, o una sal farmacéuticamente aceptable del mismo;

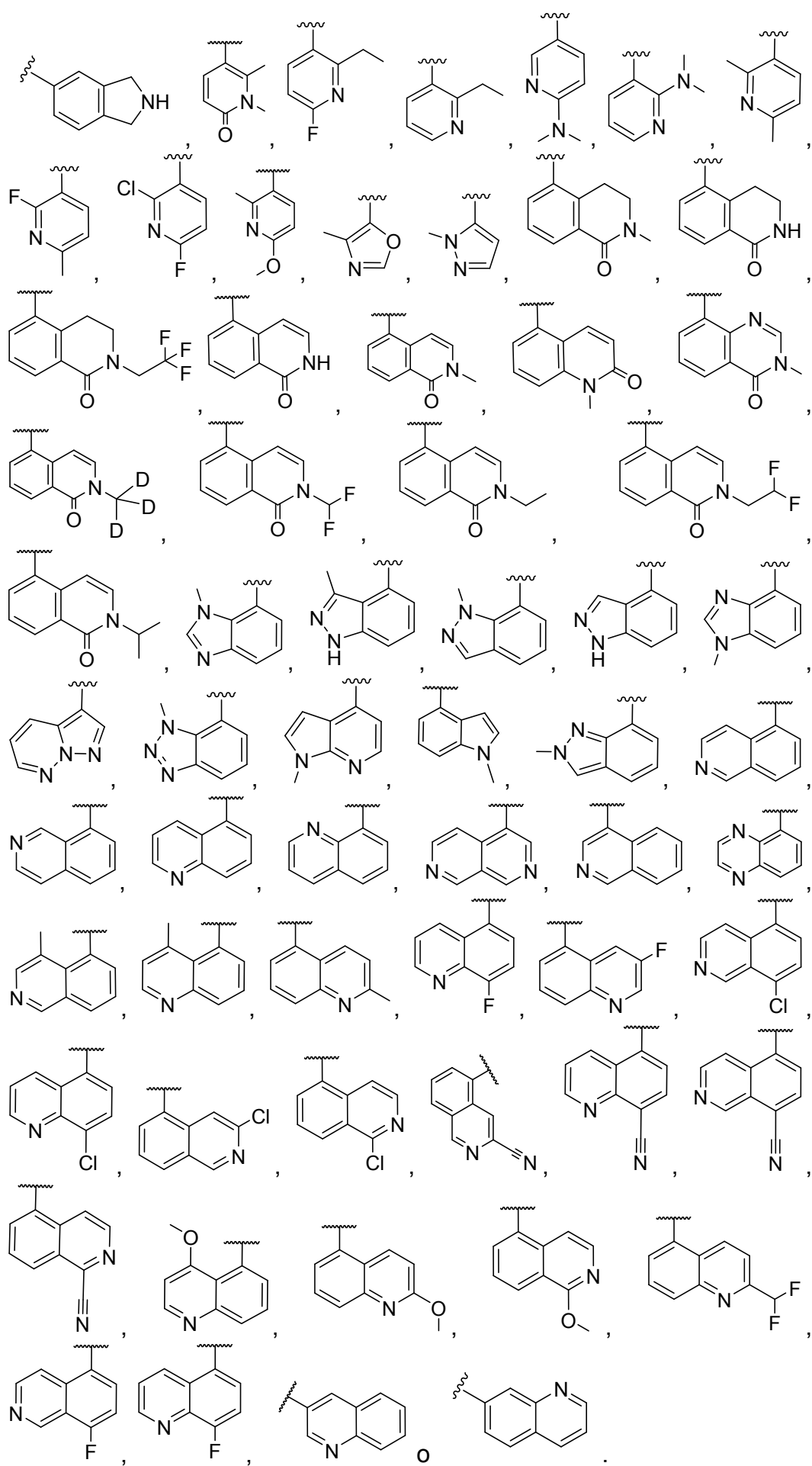




en donde cada Z^4 de (iv) a (vi) puede ser seleccionado independientemente del grupo que consiste en -CN, halo, -O- R^{12} , -C(O)- R^{12} , -N(R^{13})(R^{14}), alquilo C_{1-9} , haloalquilo C_{1-9} , y heterociclilo, o una sal farmacéuticamente aceptable del mismo;

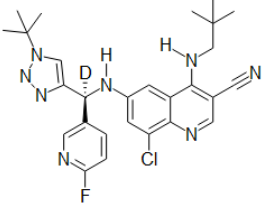
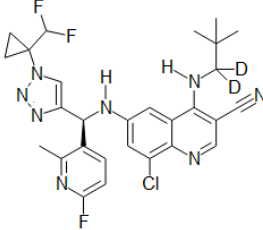
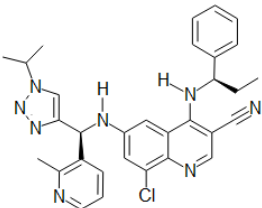
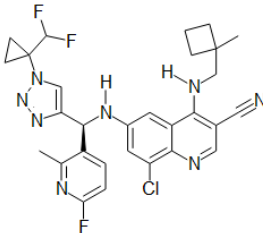
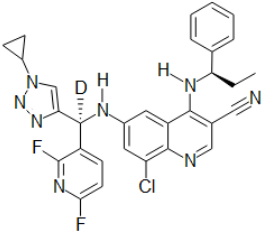
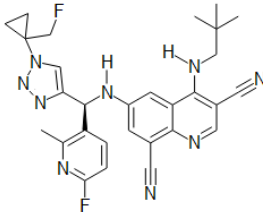
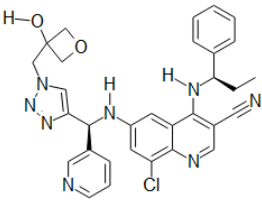
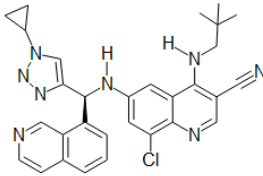
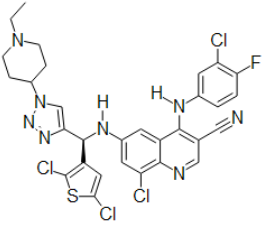
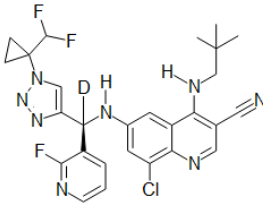






10. El compuesto de la reivindicación 1 seleccionado de la Tabla 1,

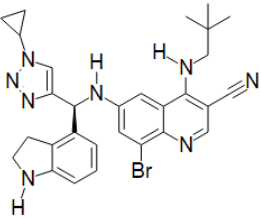
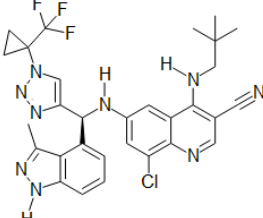
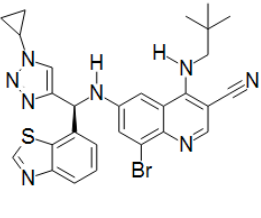
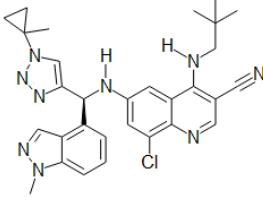
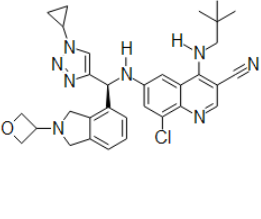
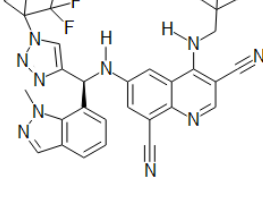
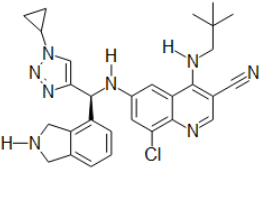
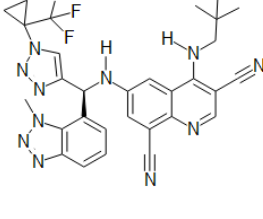
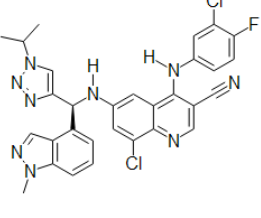
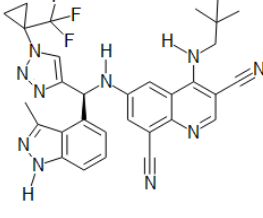
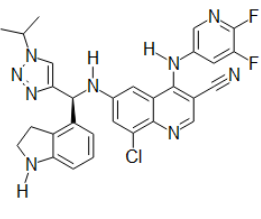
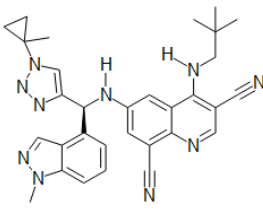
Tabla 1

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4		504	
5		505	

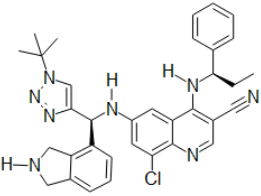
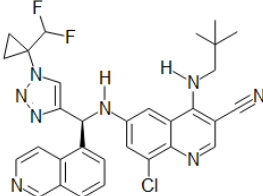
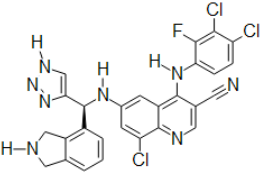
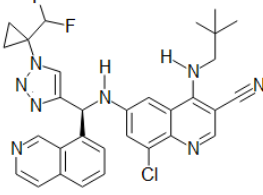
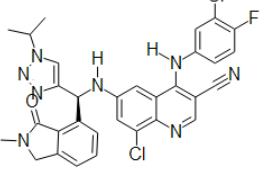
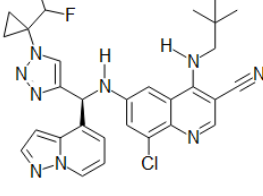
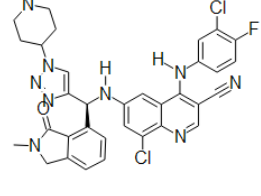
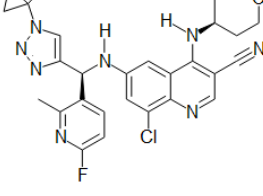
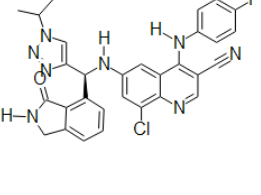
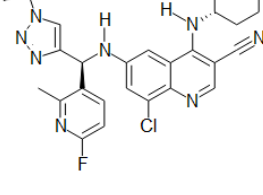
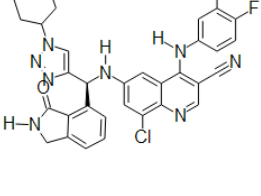
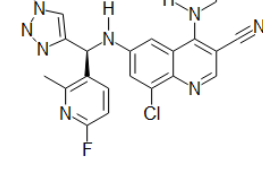
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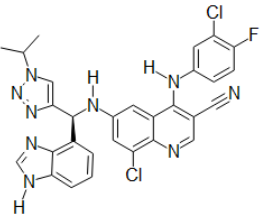
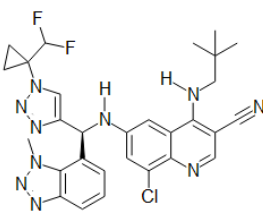
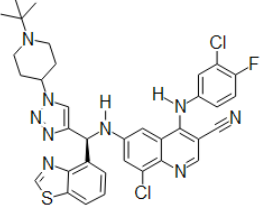
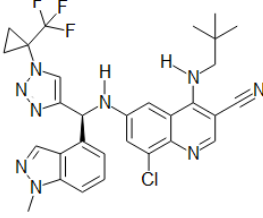
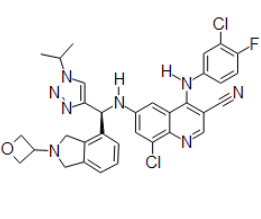
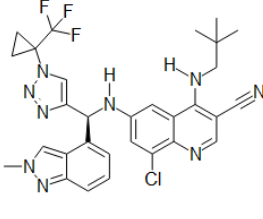
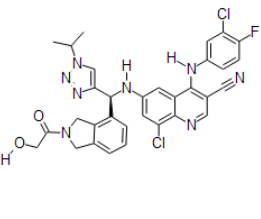
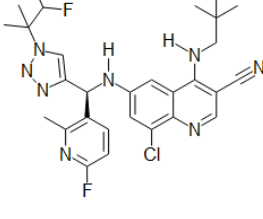
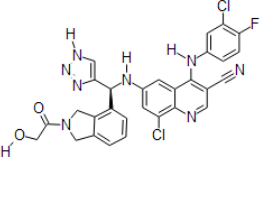
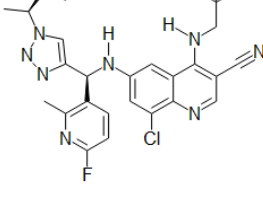
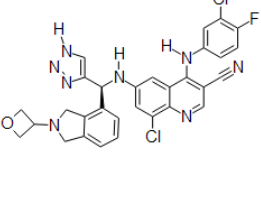
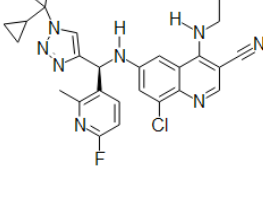
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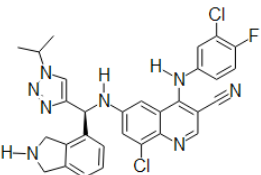
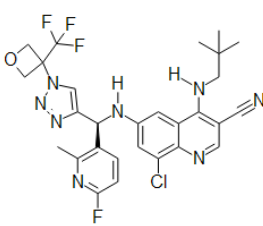
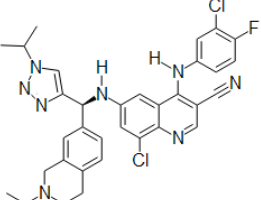
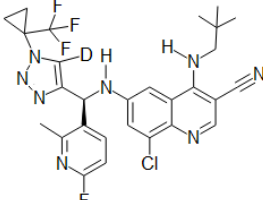
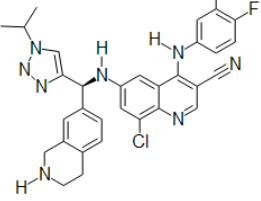
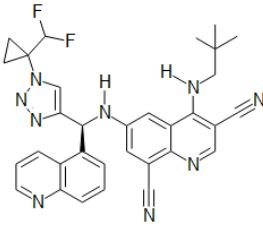
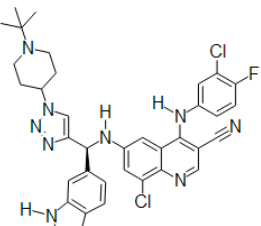
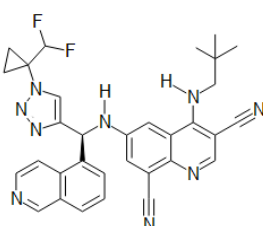
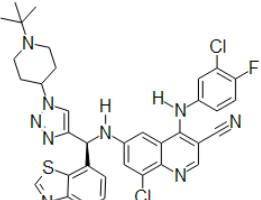
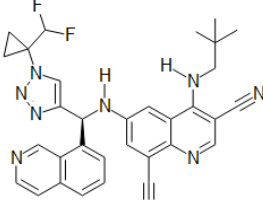
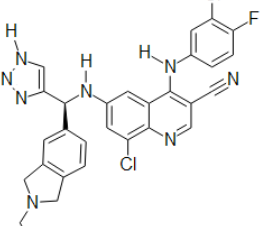
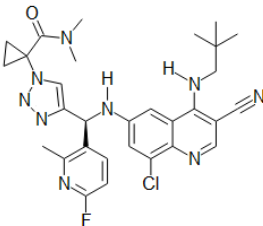
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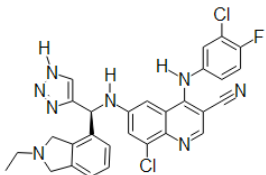
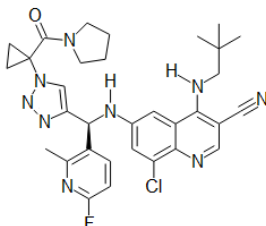
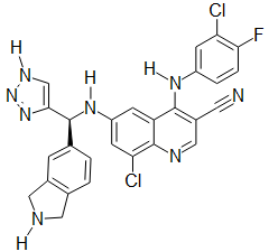
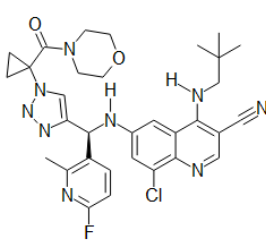
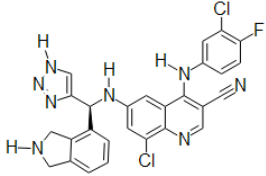
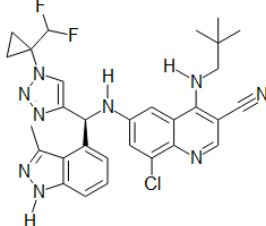
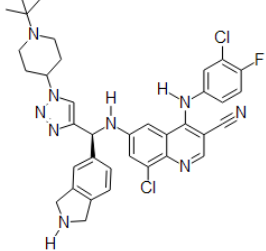
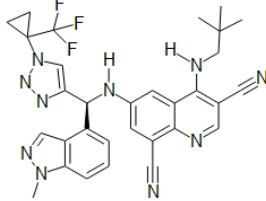
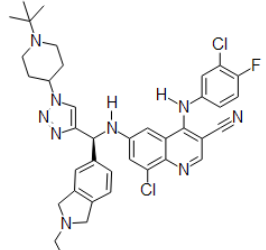
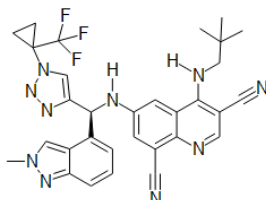
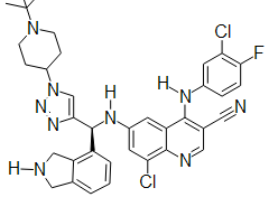
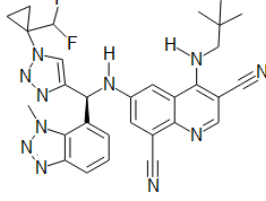
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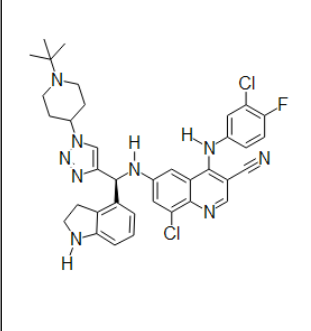
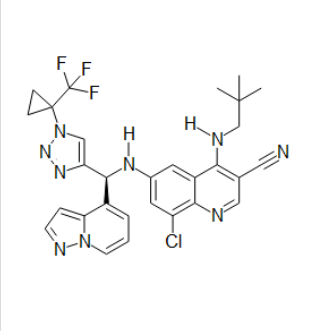
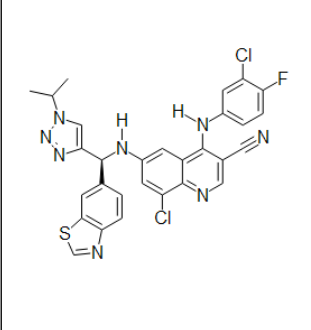
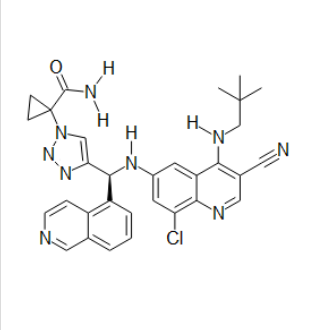
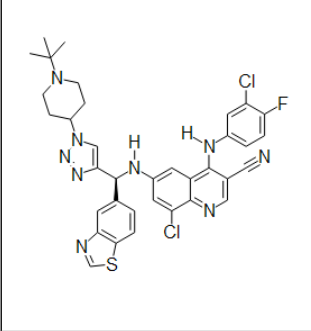
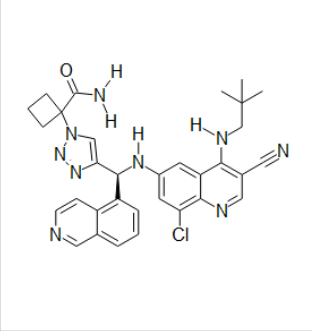
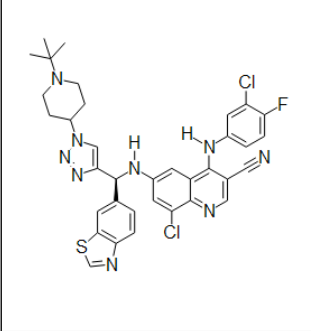
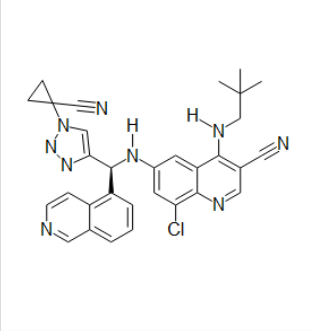
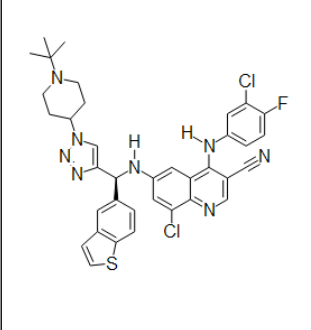
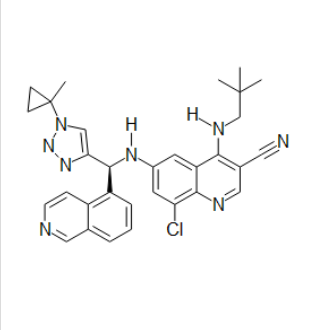
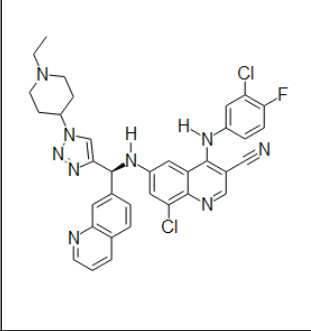
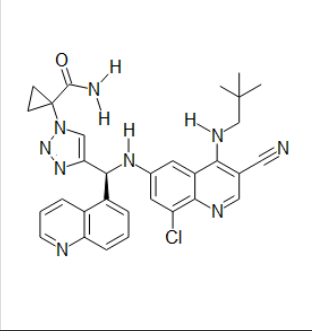
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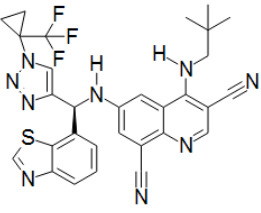
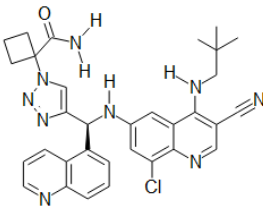
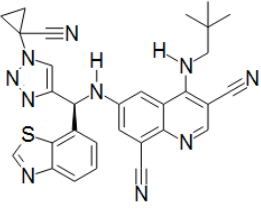
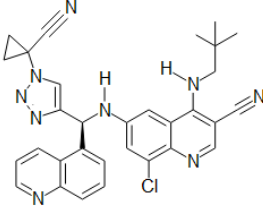
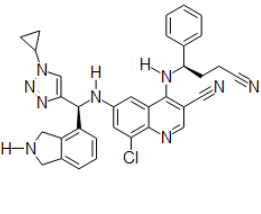
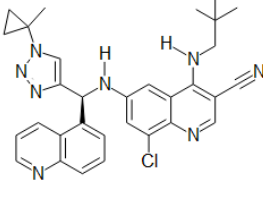
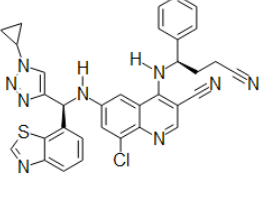
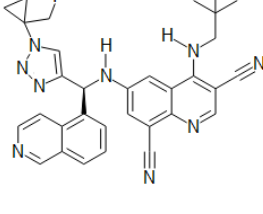
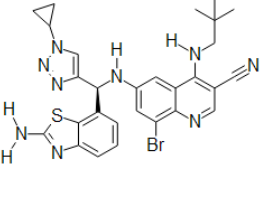
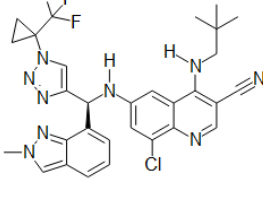
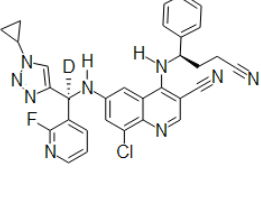
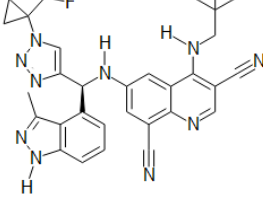
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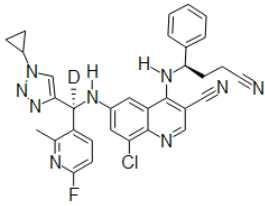
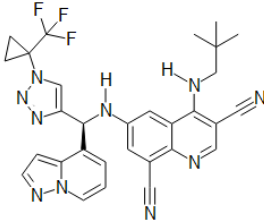
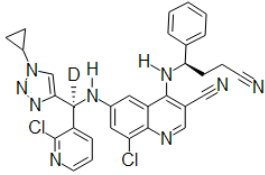
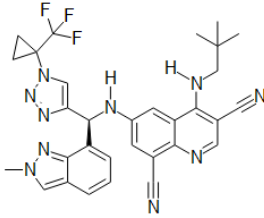
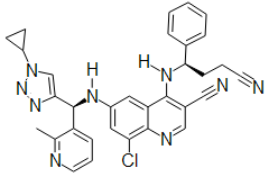
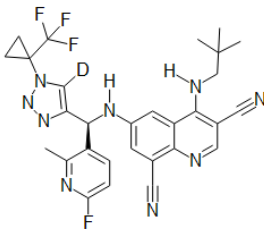
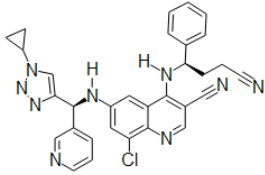
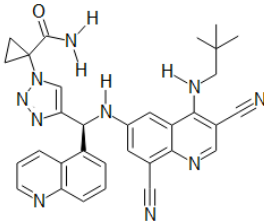
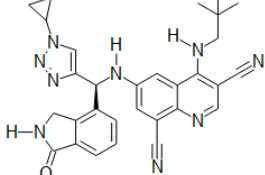
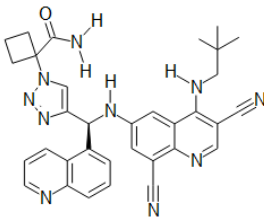
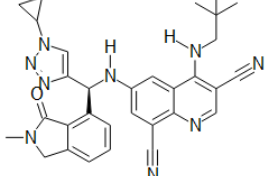
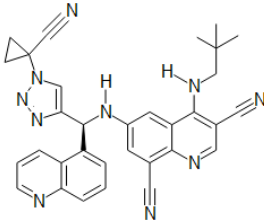
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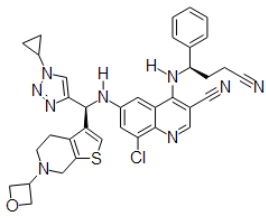
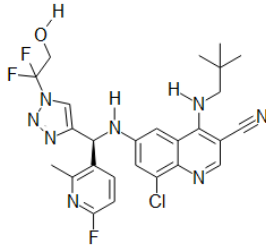
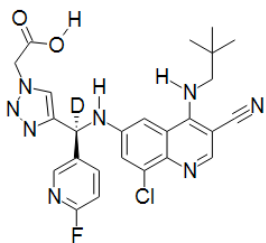
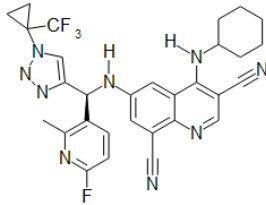
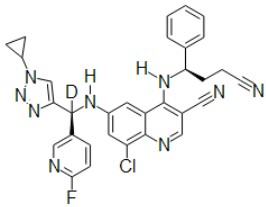
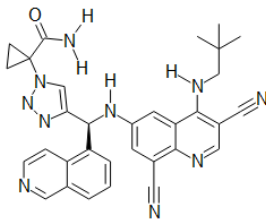
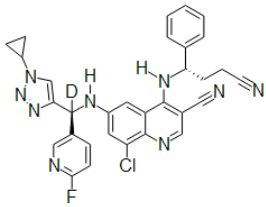
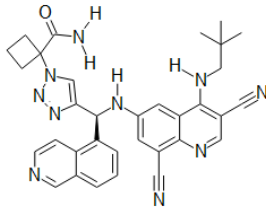
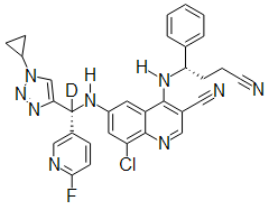
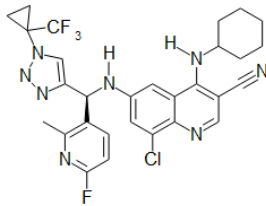
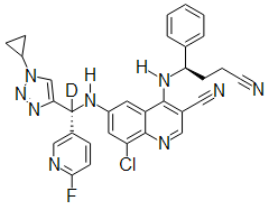
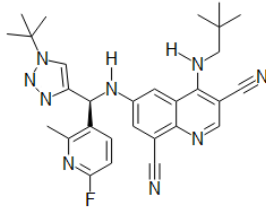
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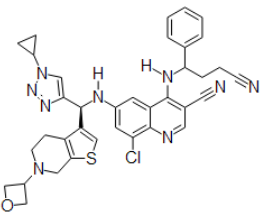
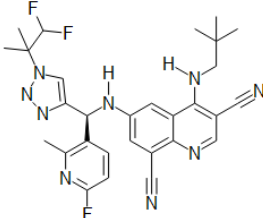
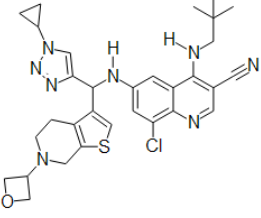
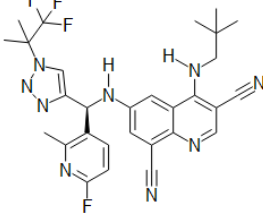
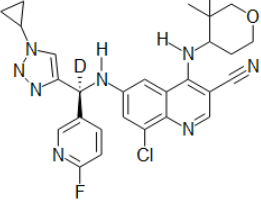
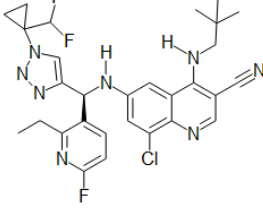
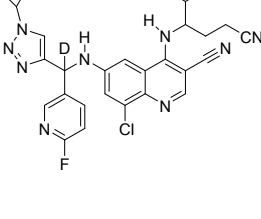
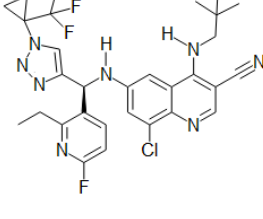
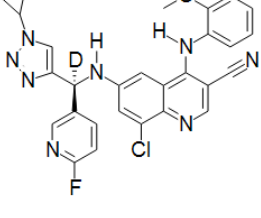
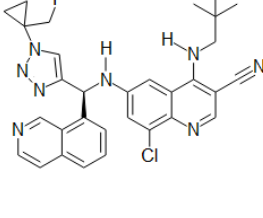
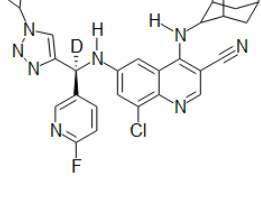
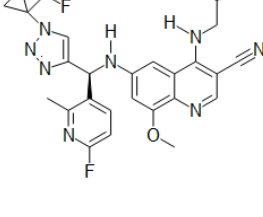
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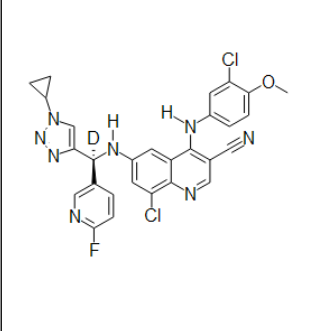
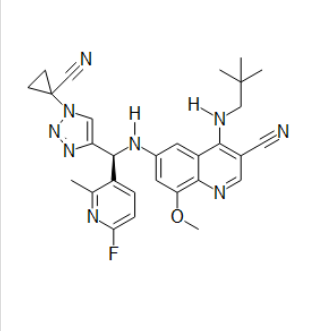
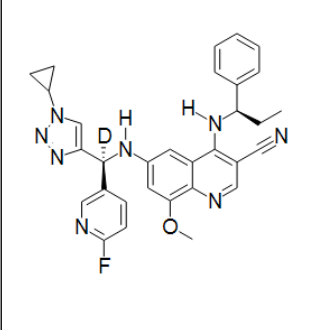
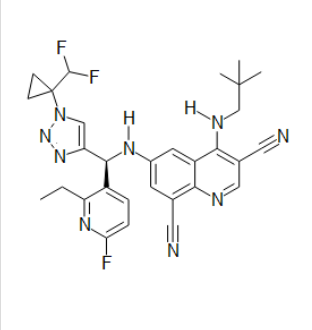
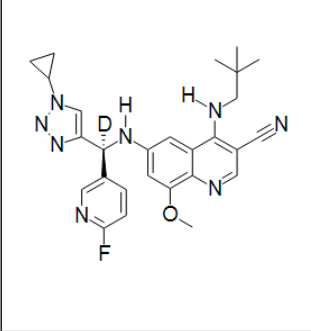
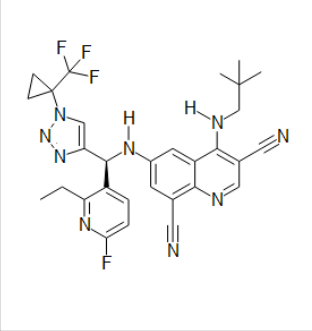
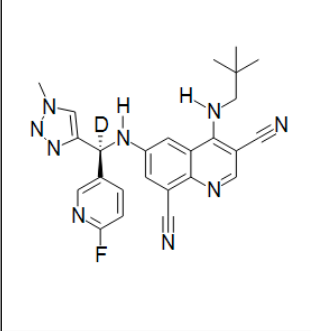
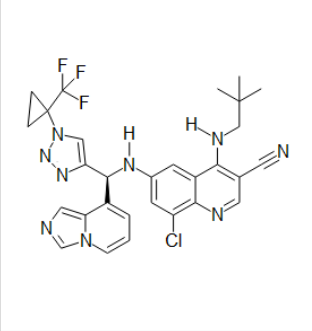
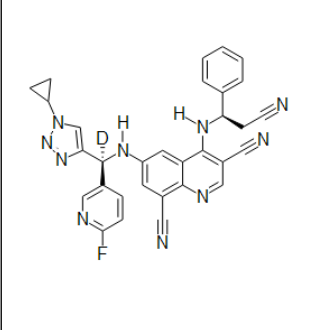
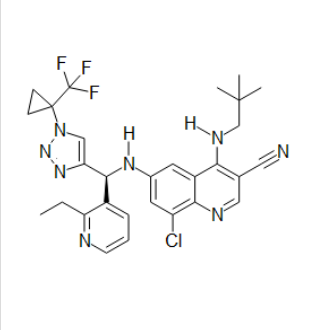
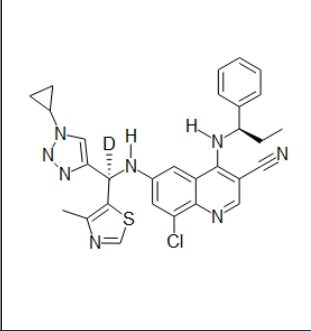
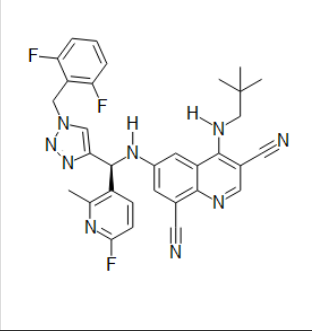
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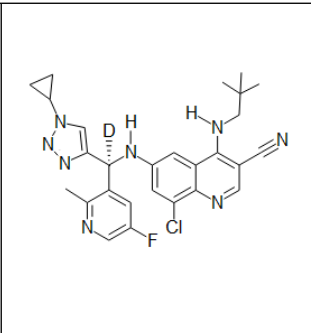
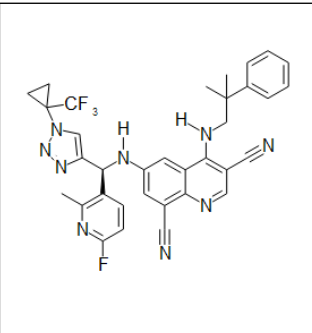
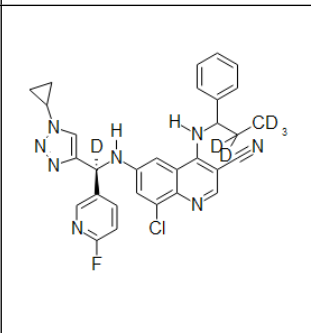
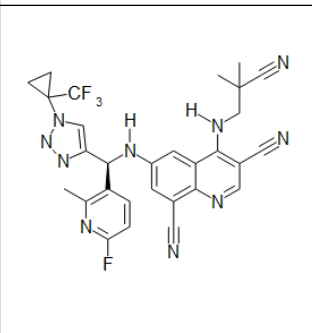
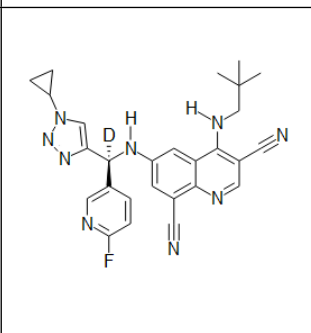
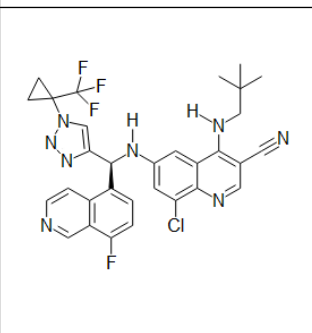
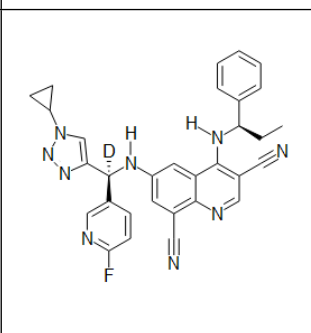
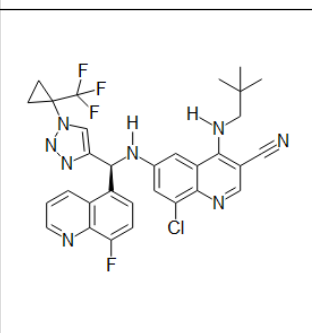
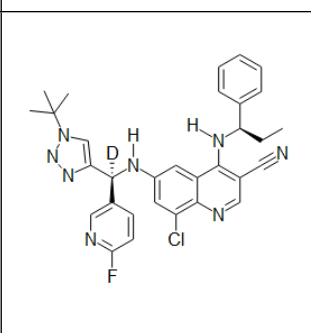
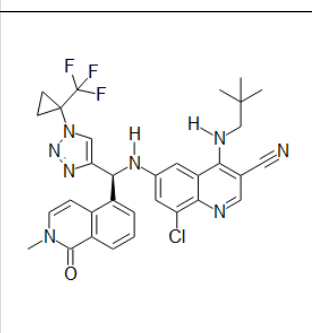
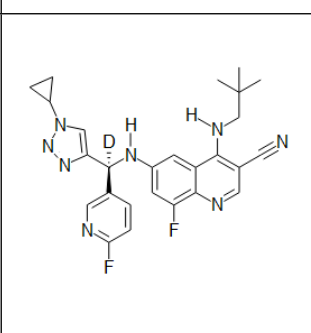
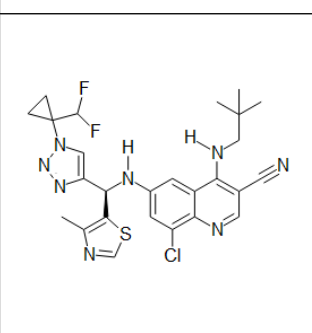
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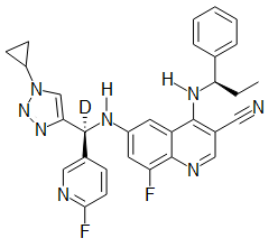
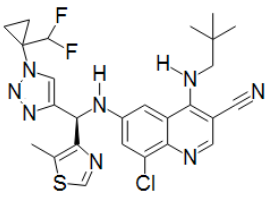
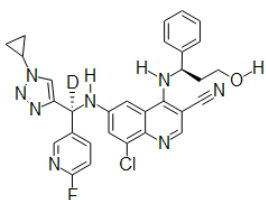
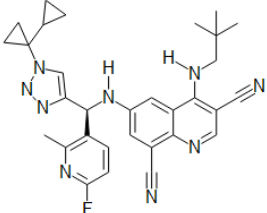
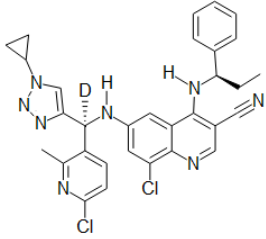
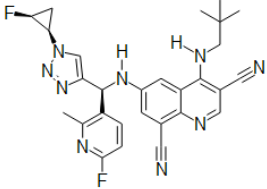
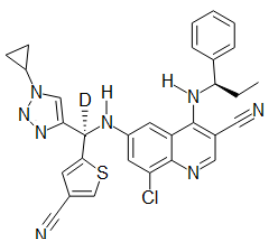
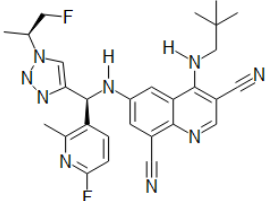
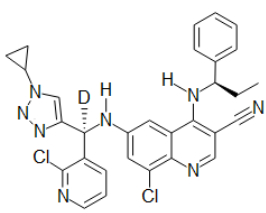
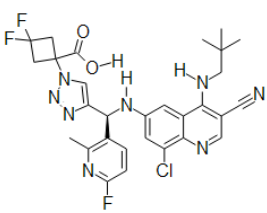
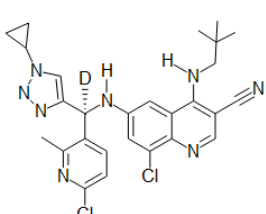
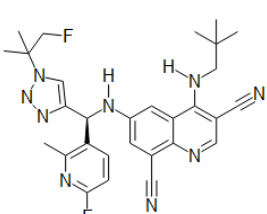
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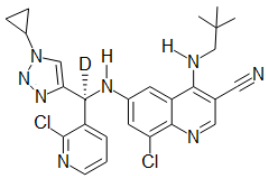
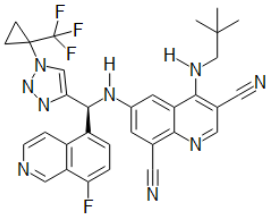
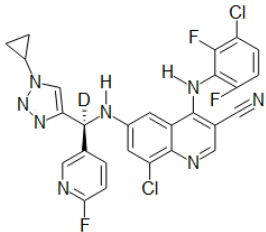
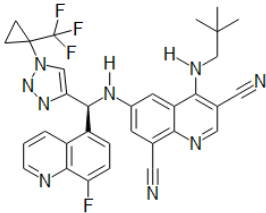
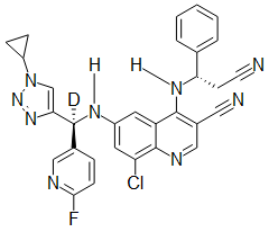
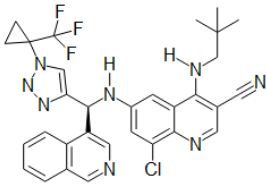
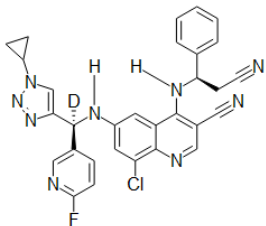
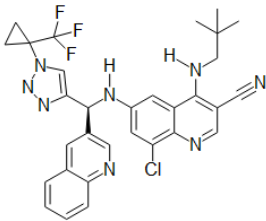
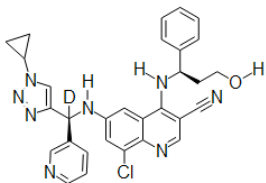
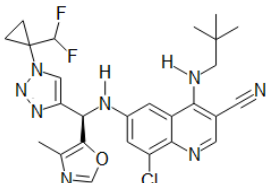
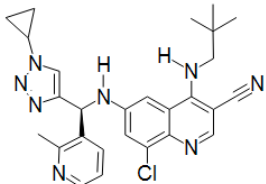
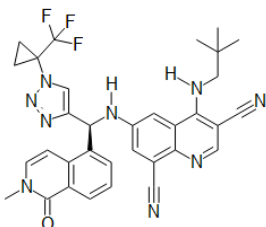
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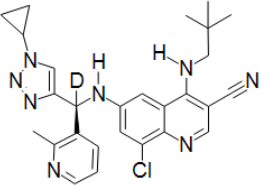
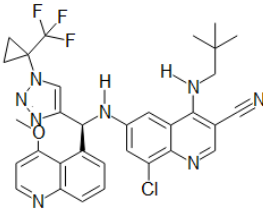
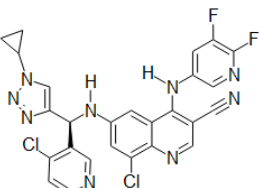
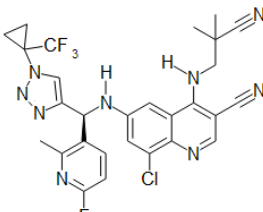
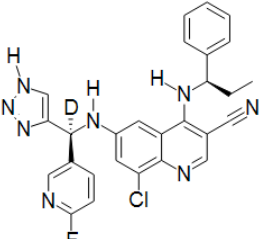
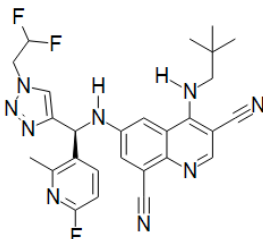
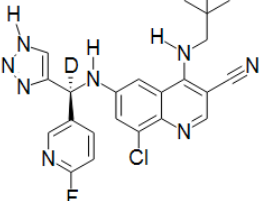
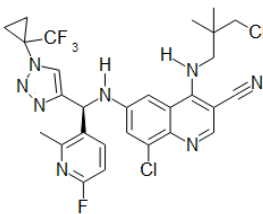
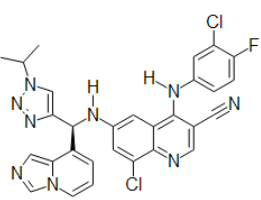
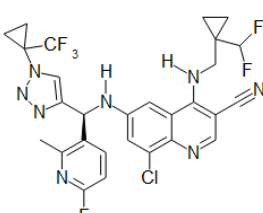
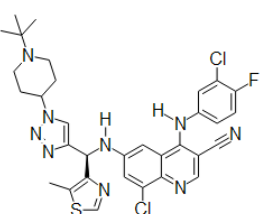
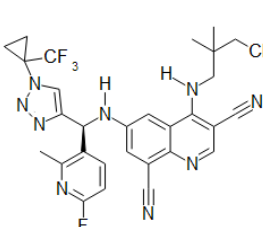
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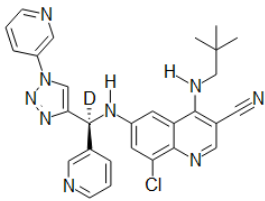
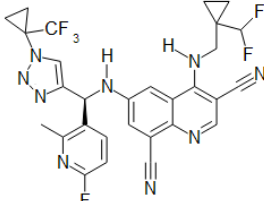
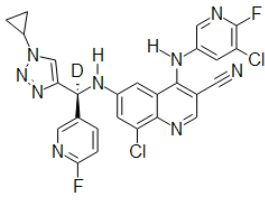
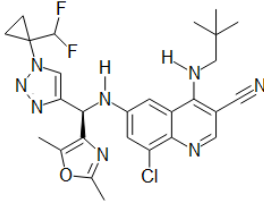
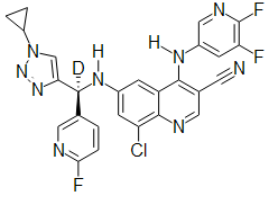
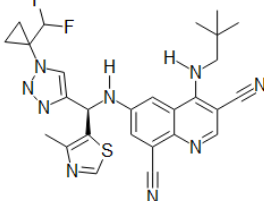
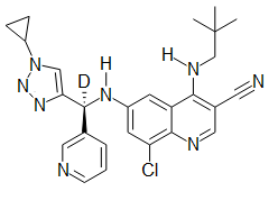
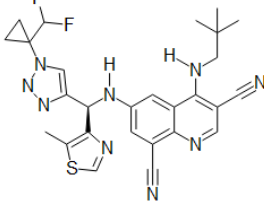
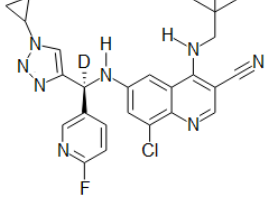
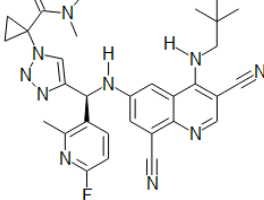
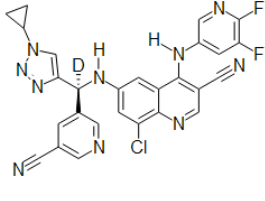
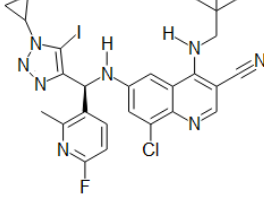
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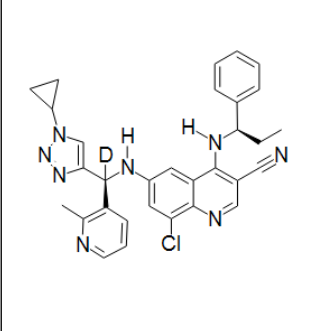
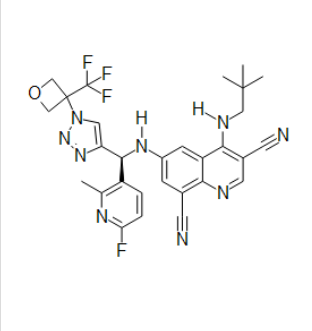
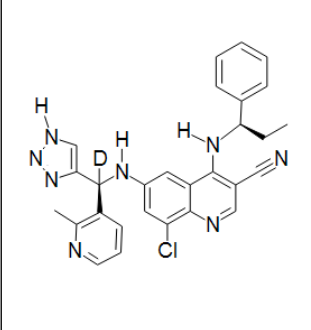
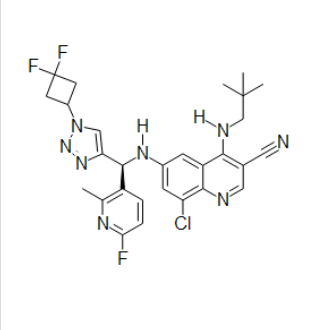
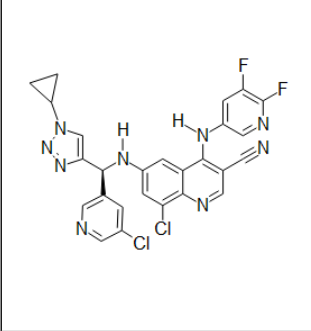
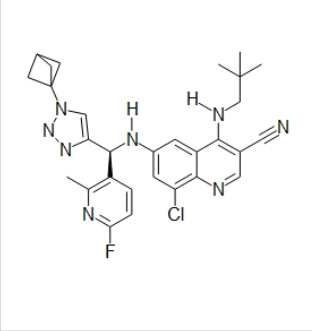
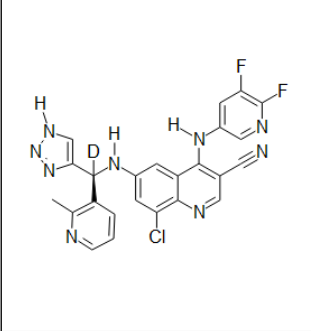
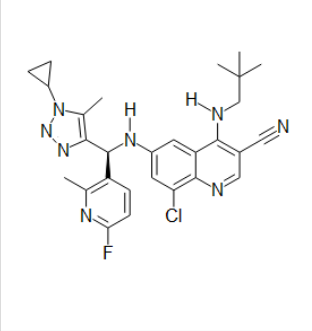
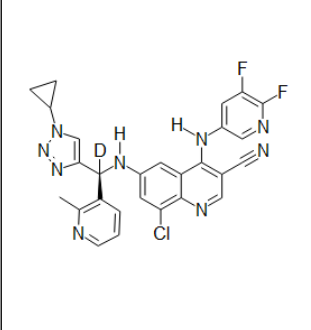
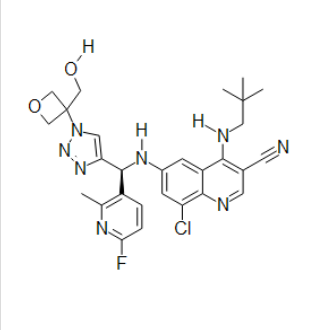
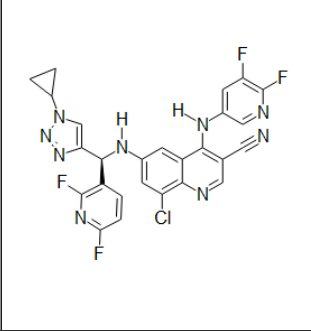
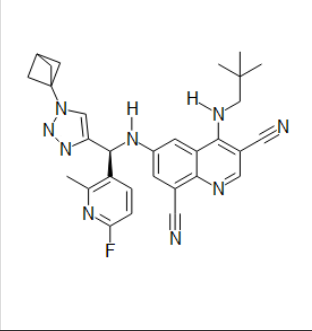
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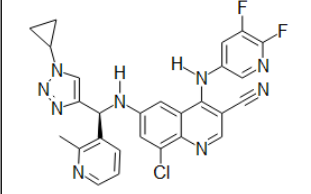
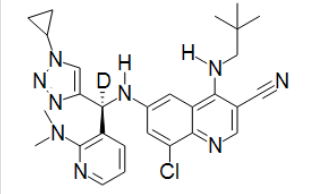
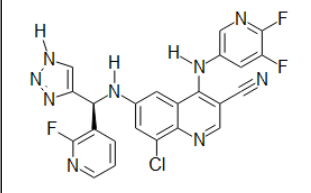
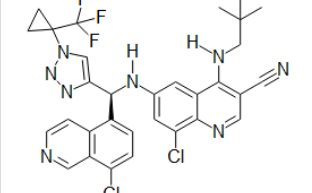
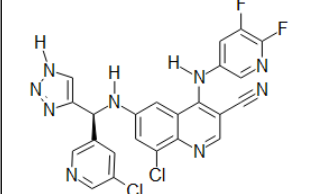
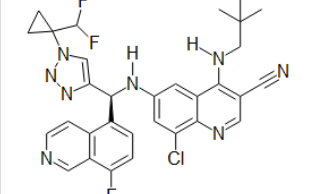
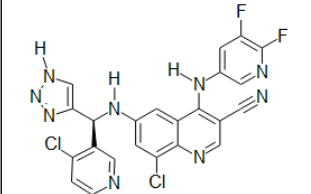
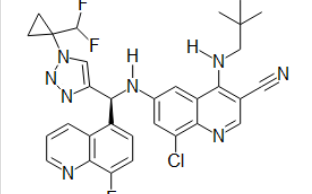
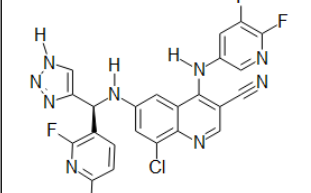
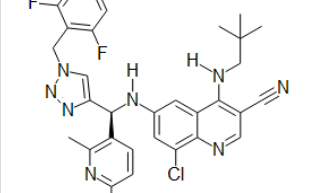
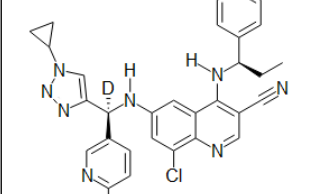
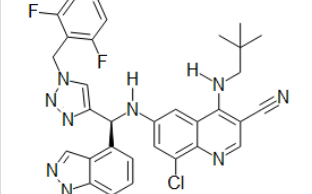
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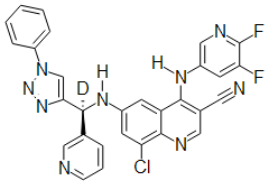
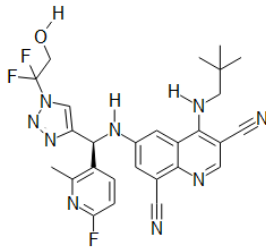
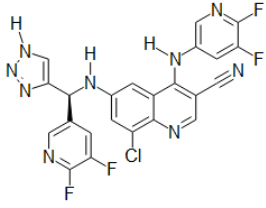
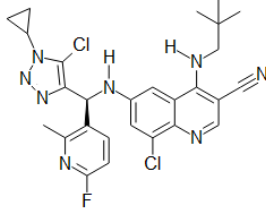
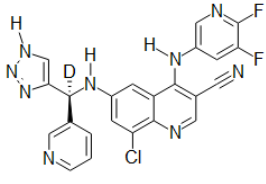
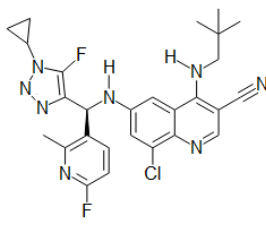
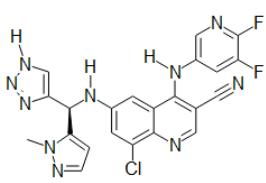
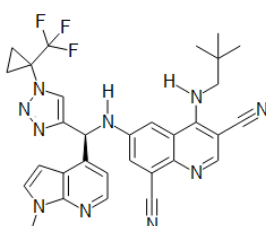
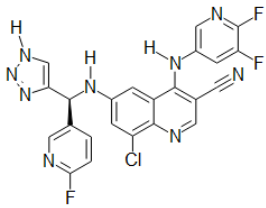
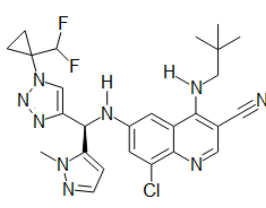
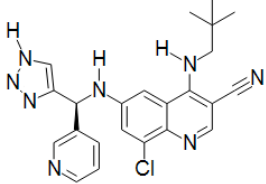
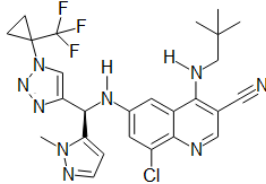
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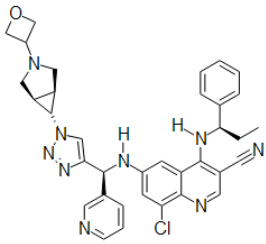
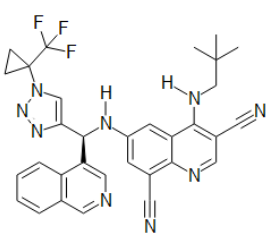
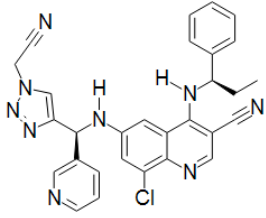
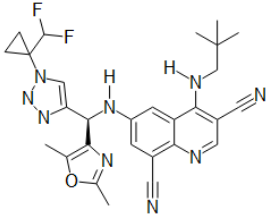
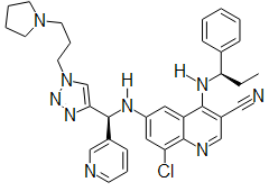
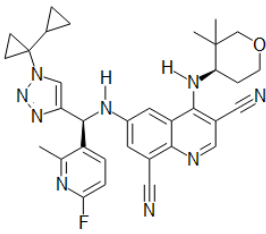
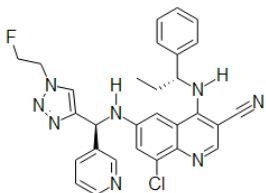
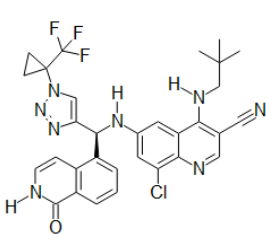
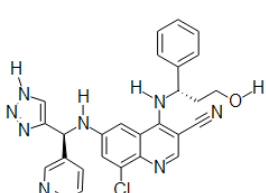
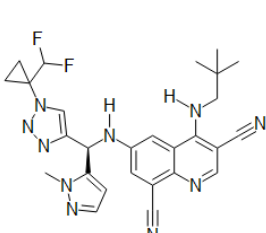
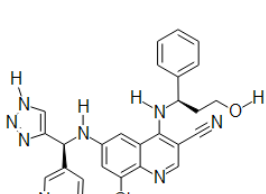
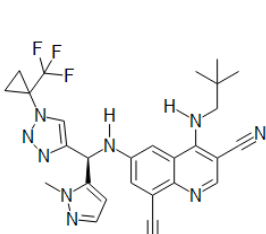
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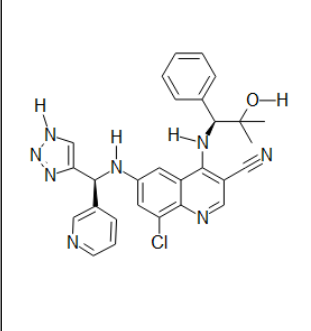
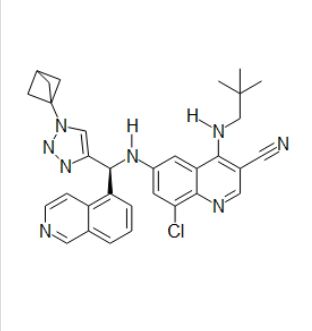
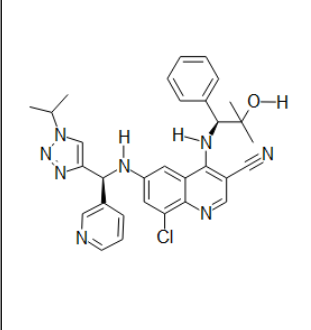
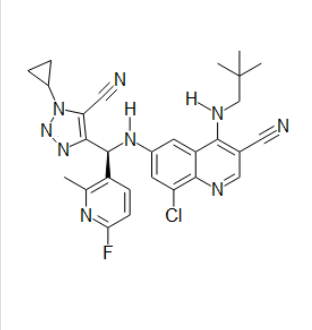
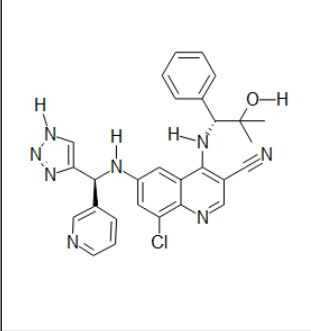
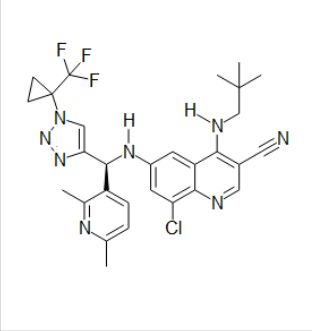
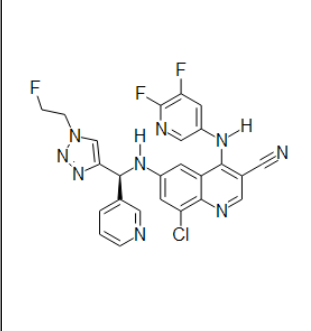
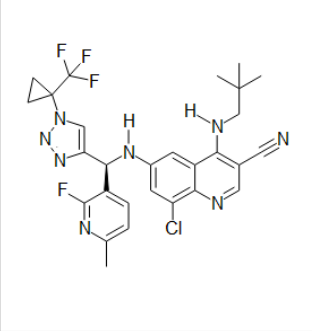
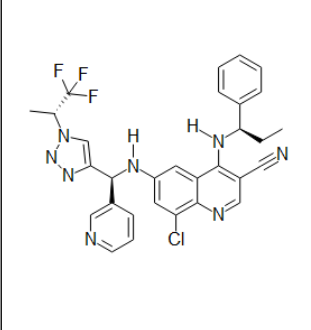
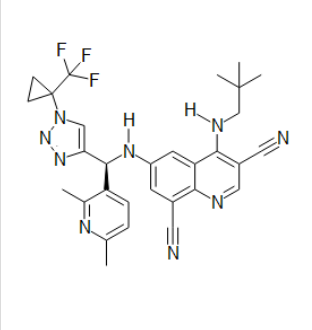
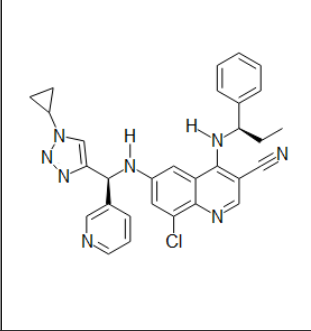
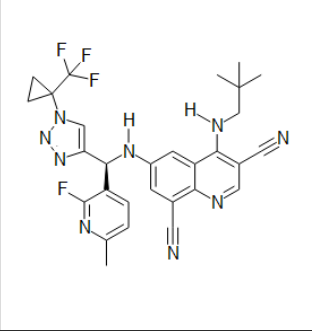
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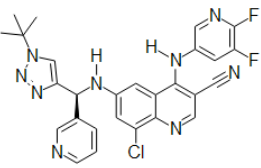
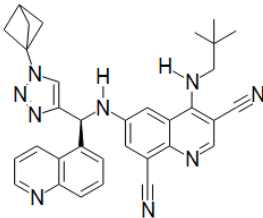
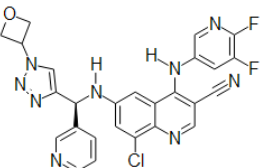
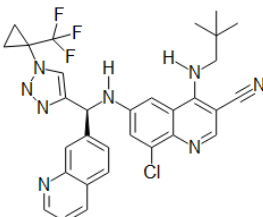
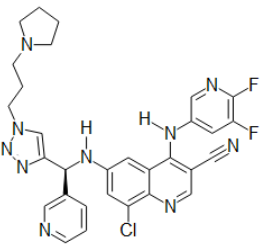
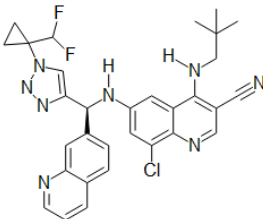
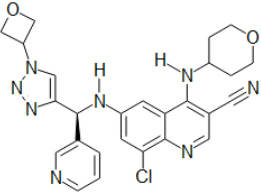
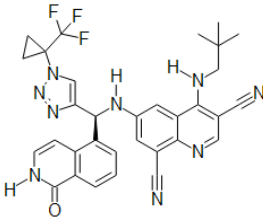
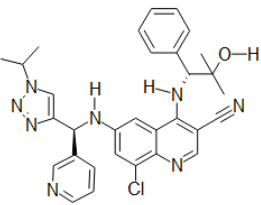
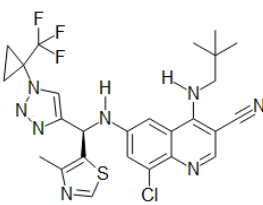
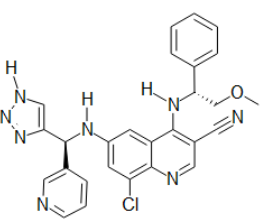
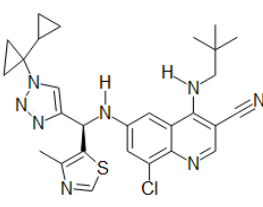
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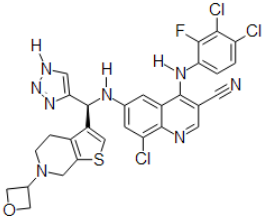
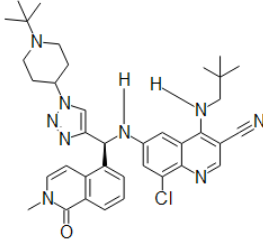
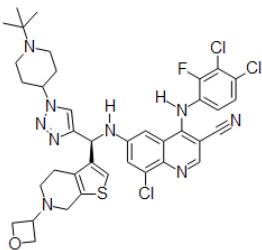
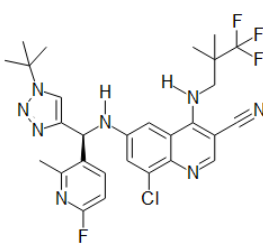
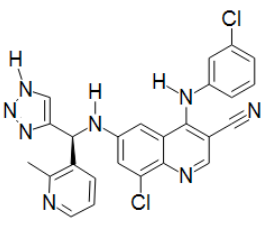
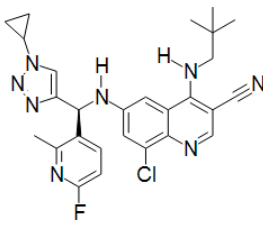
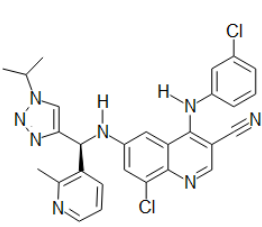
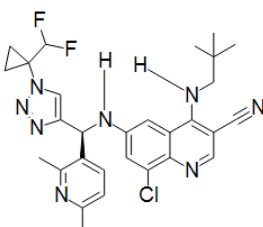
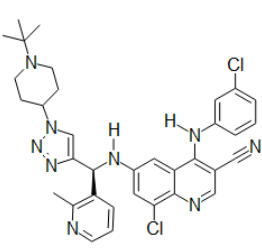
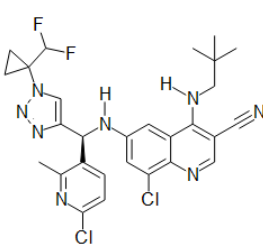
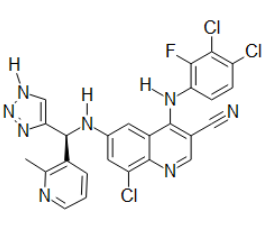
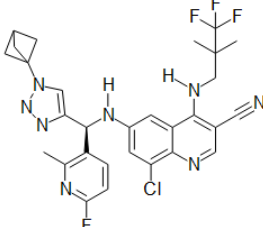
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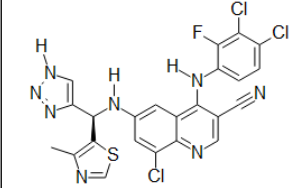
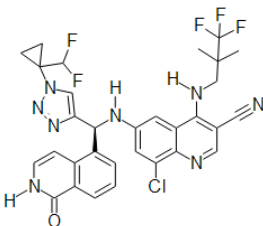
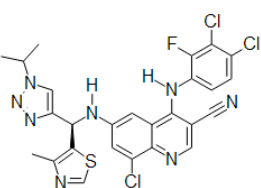
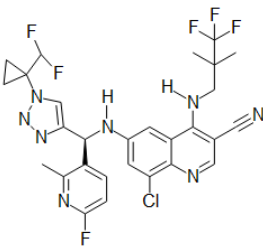
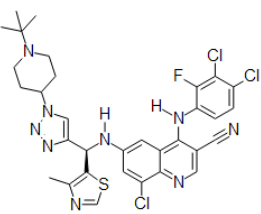
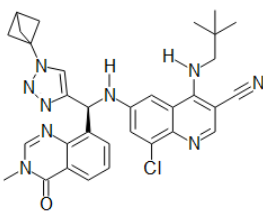
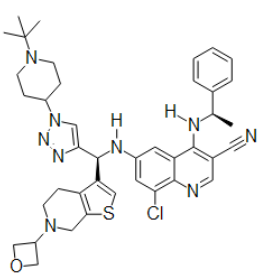
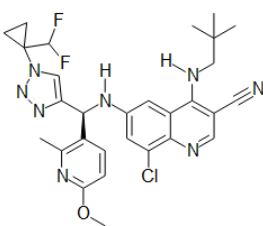
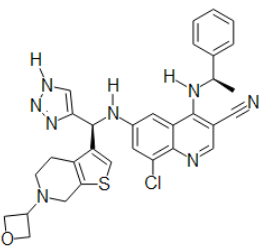
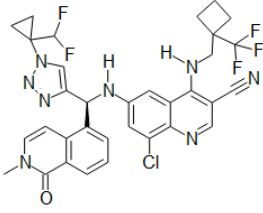
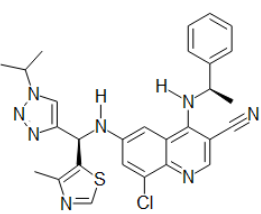
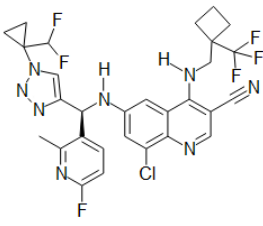
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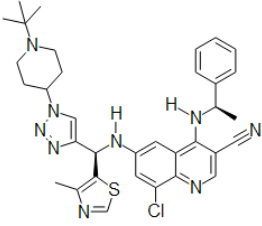
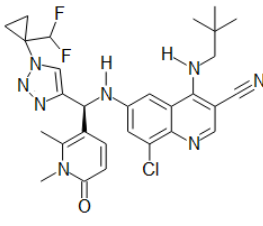
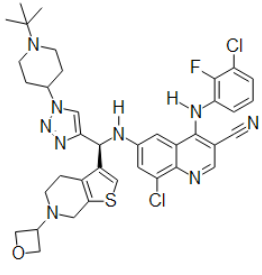
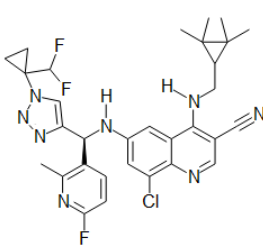
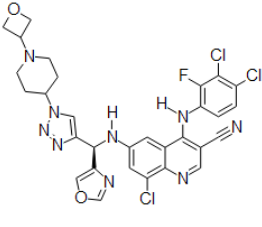
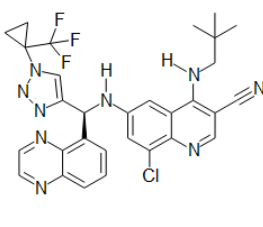
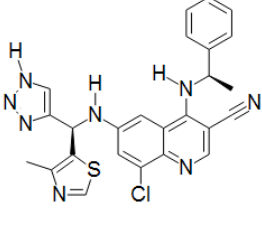
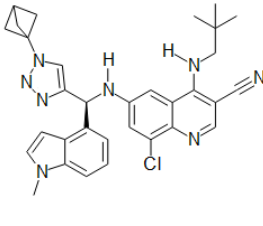
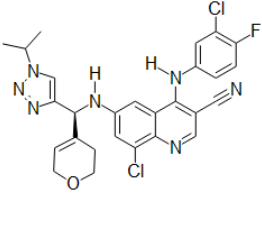
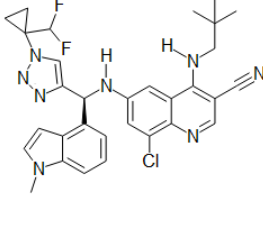
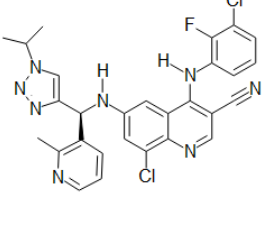
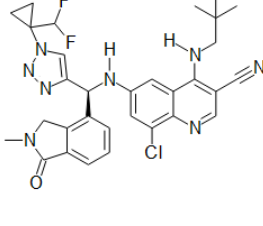
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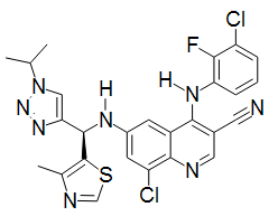
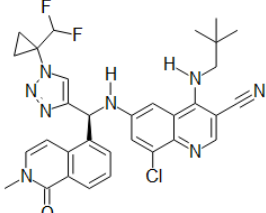
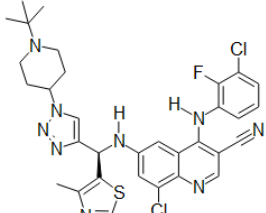
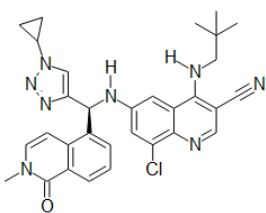
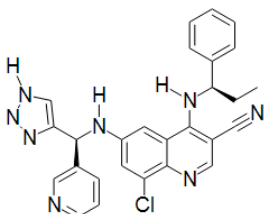
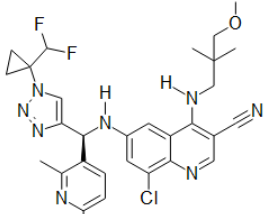
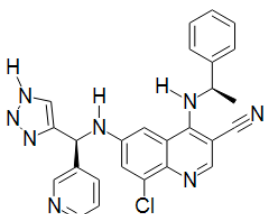
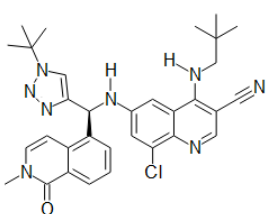
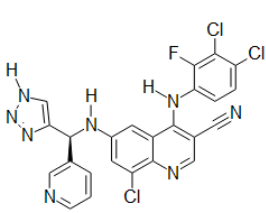
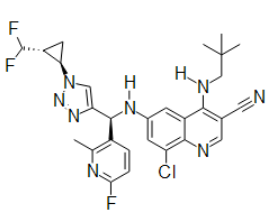
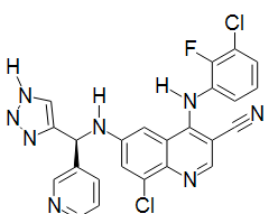
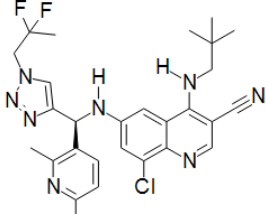
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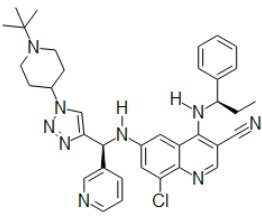
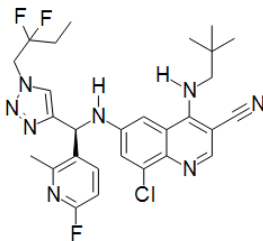
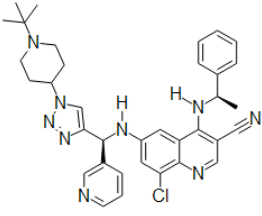
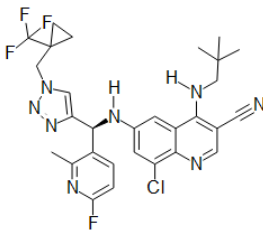
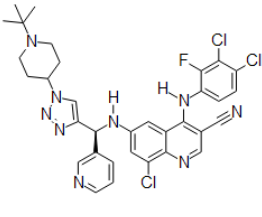
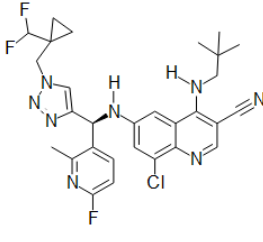
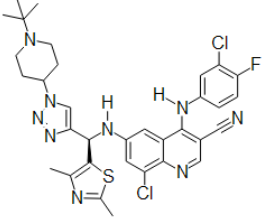
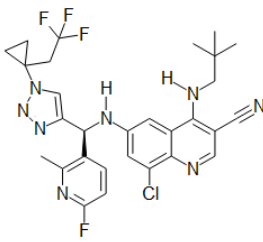
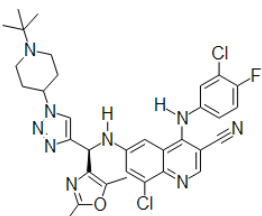
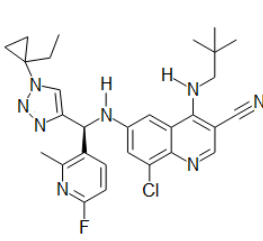
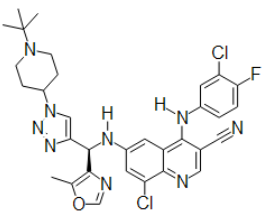
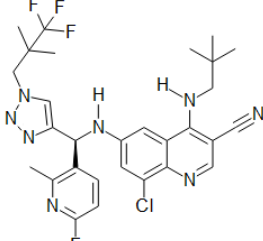
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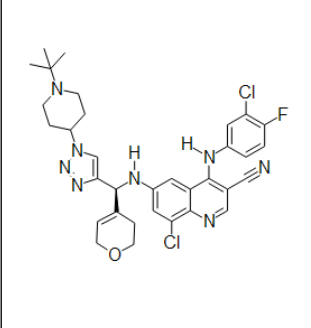
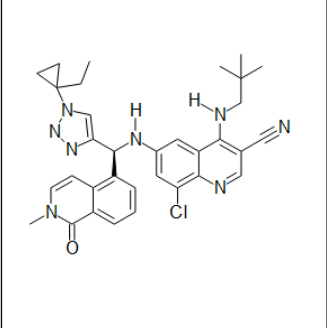
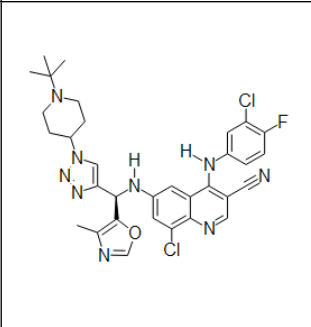
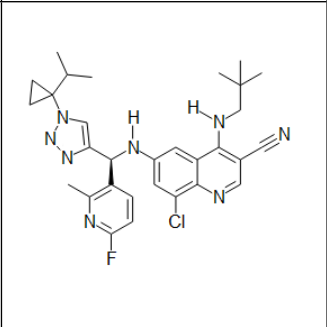
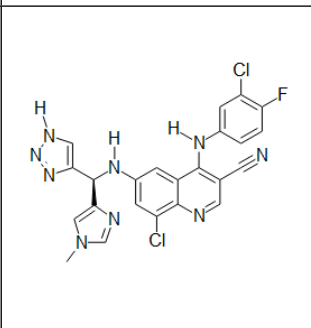
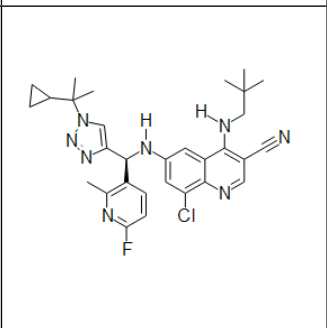
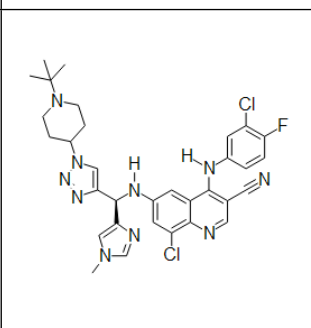
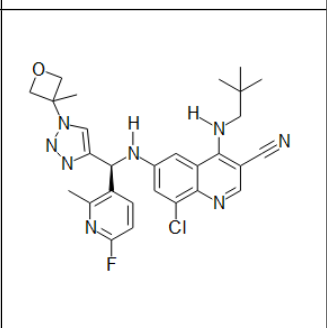
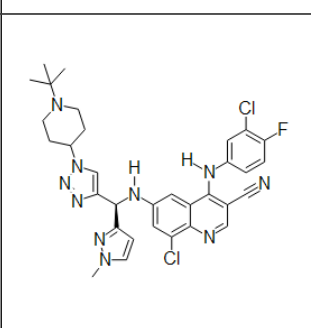
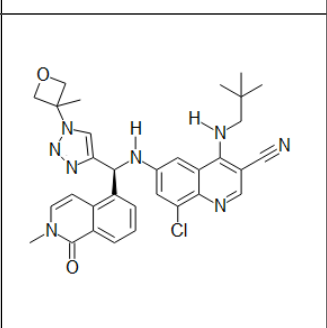
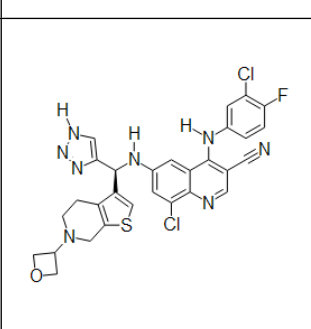
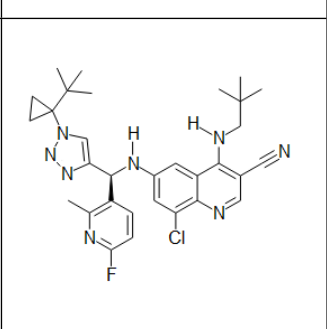
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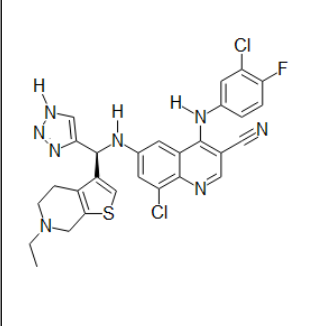
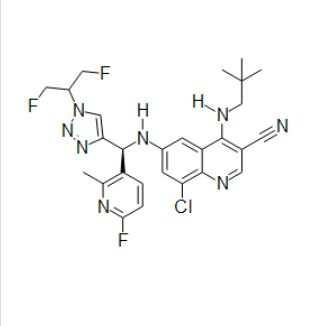
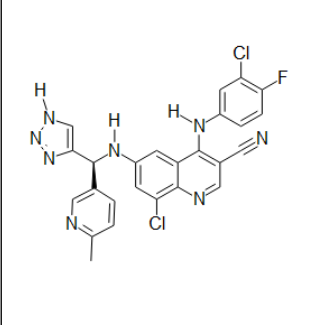
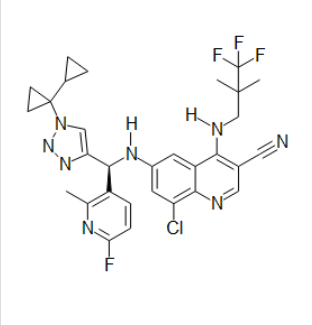
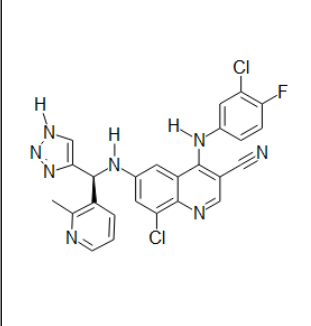
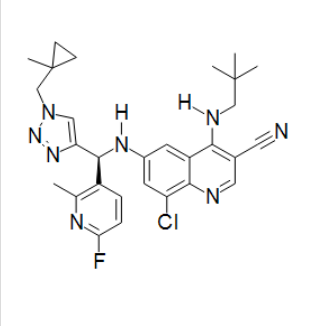
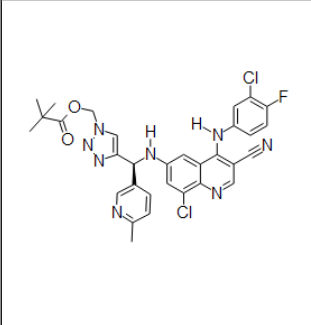
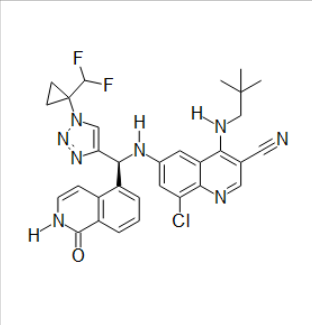
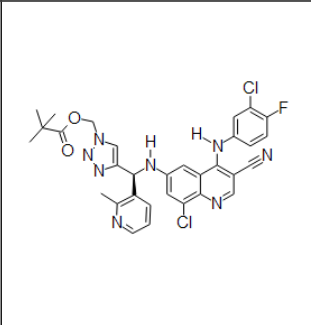
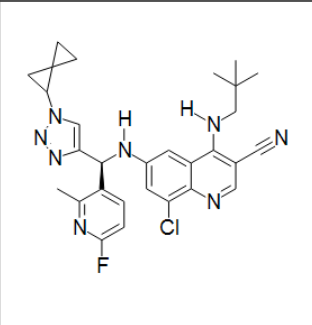
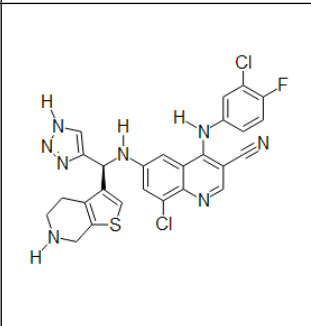
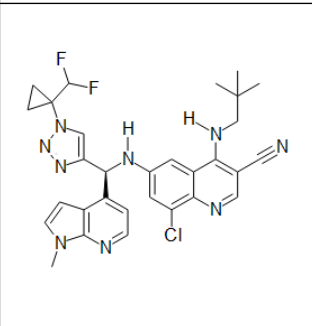
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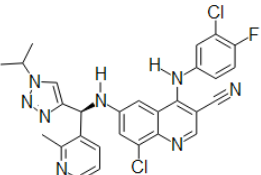
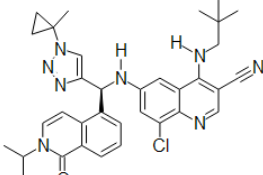
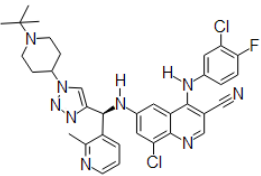
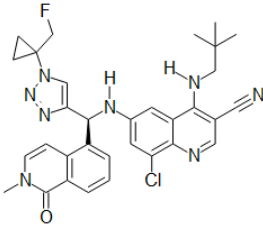
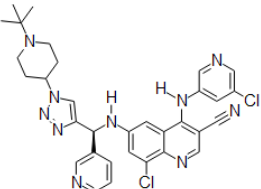
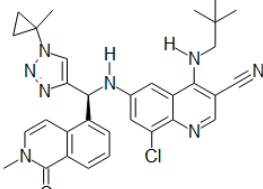
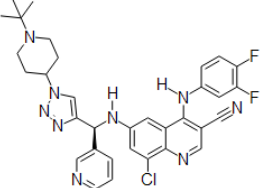
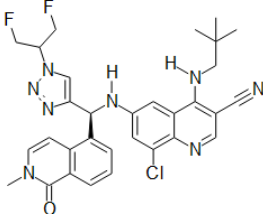
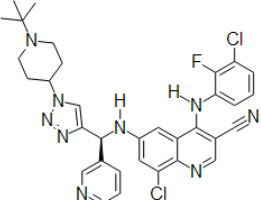
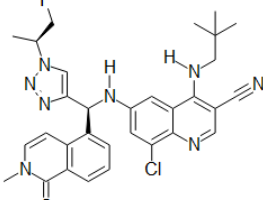
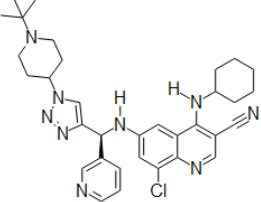
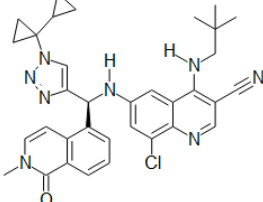
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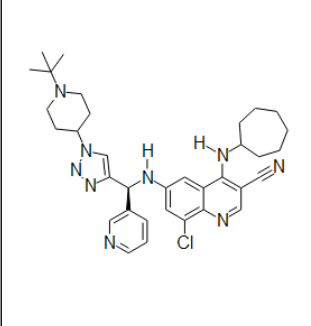
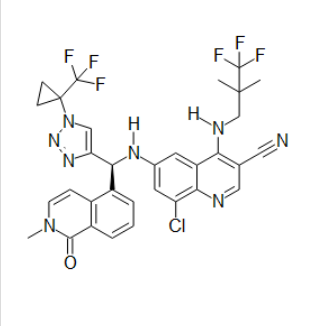
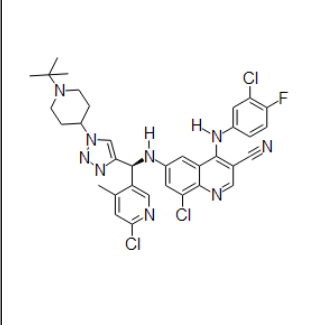
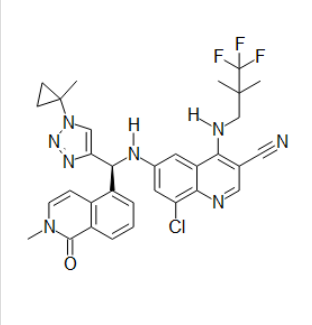
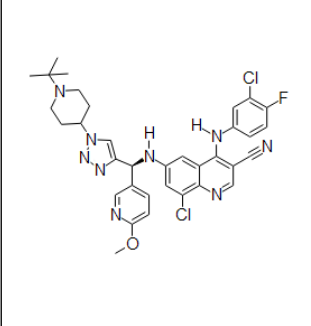
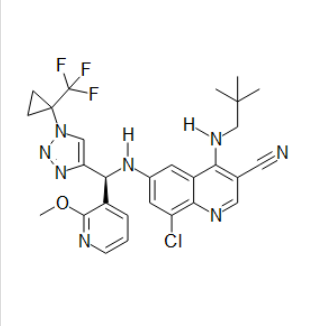
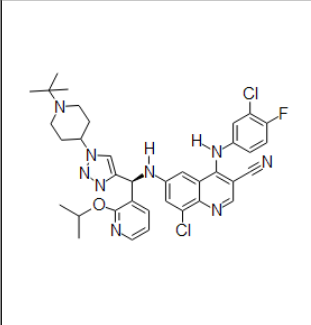
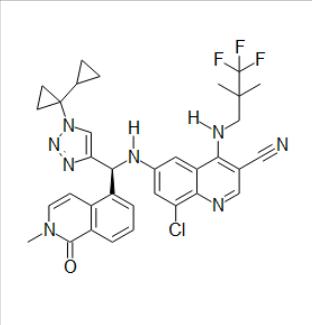
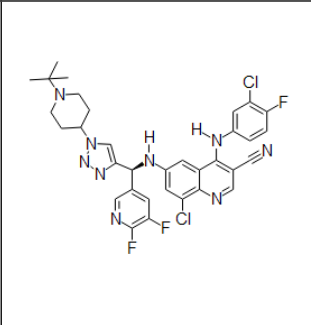
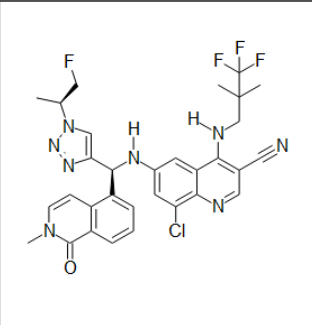
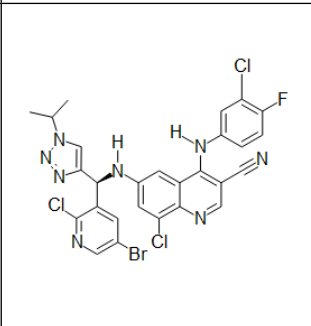
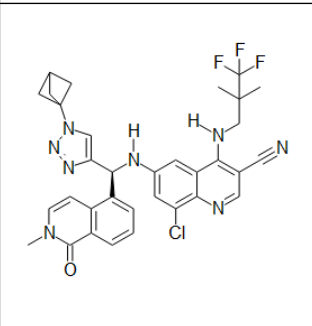
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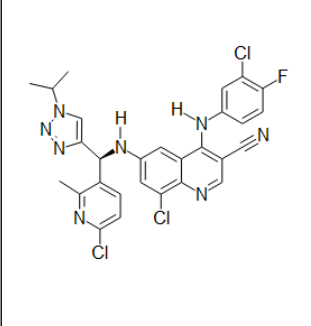
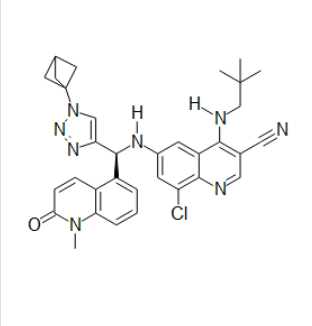
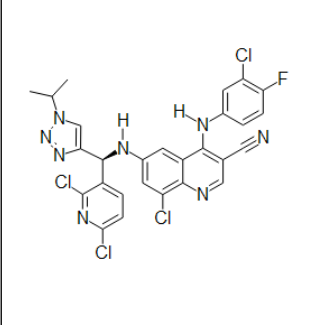
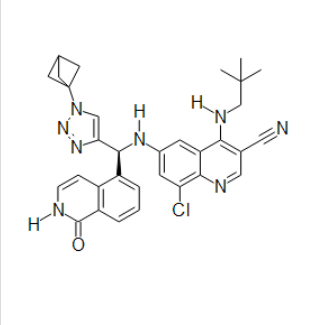
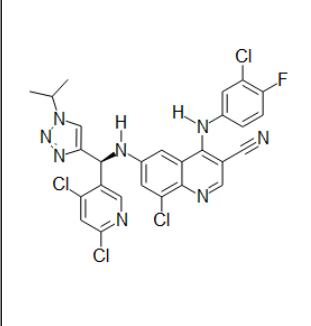
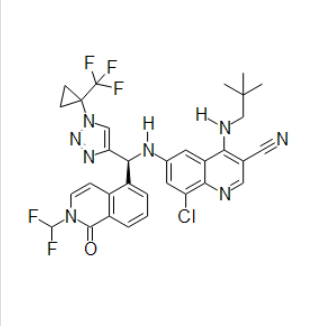
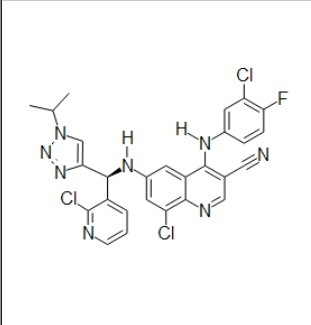
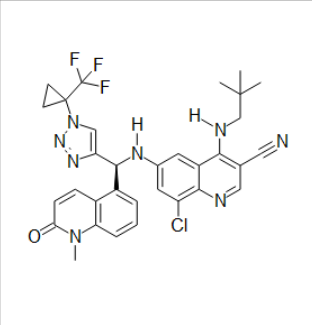
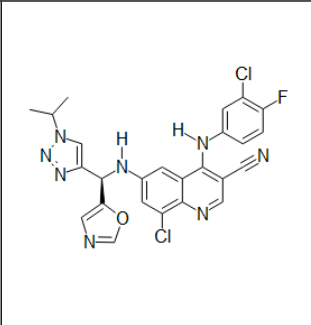
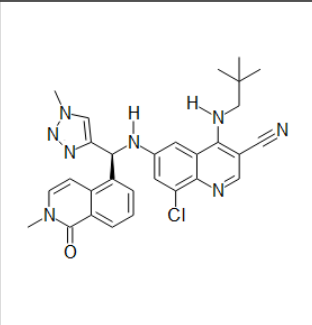
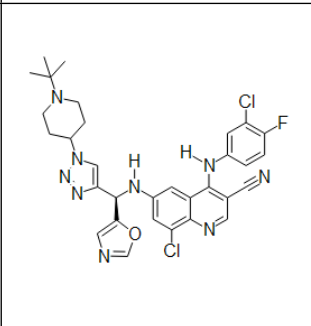
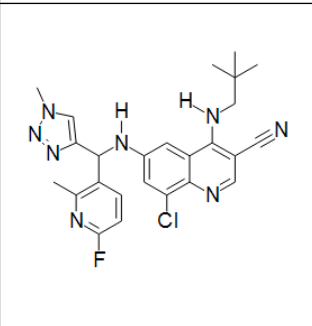
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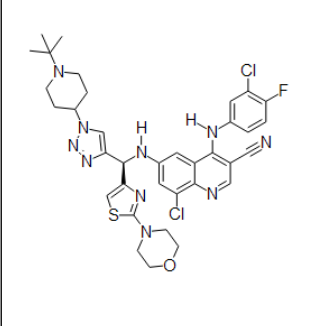
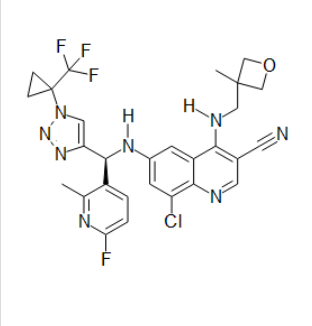
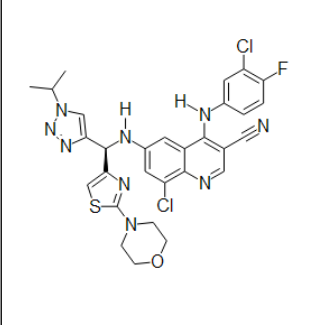
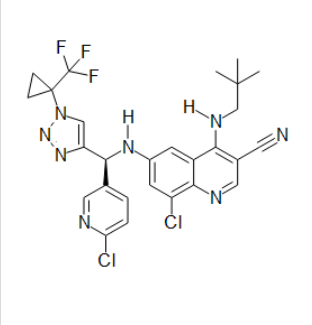
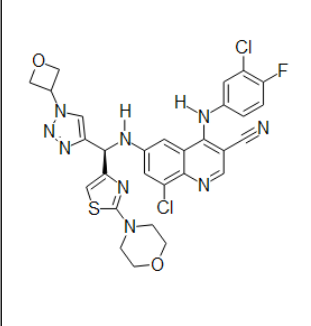
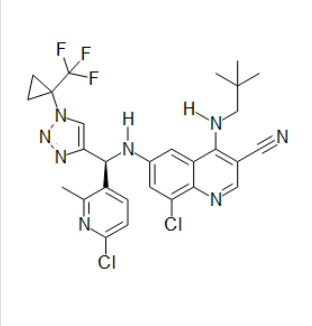
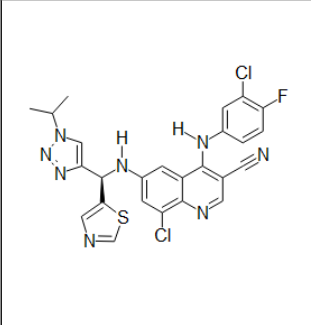
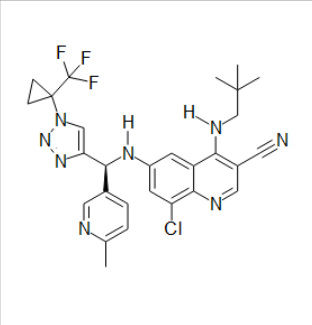
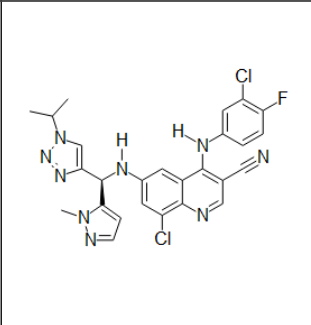
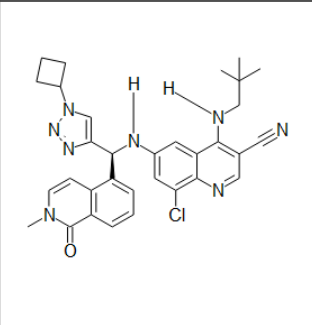
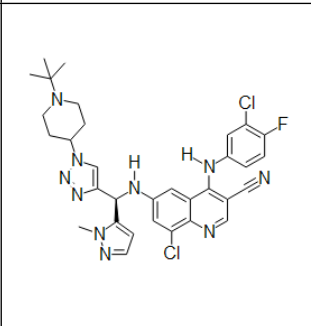
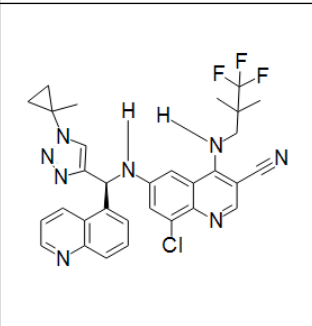
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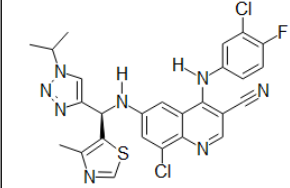
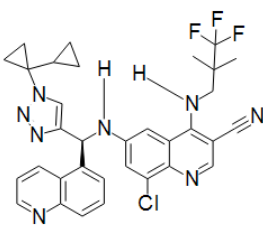
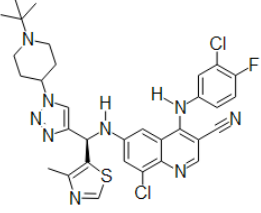
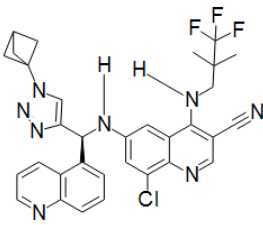
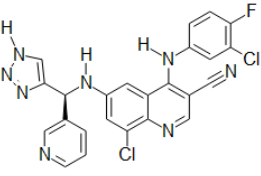
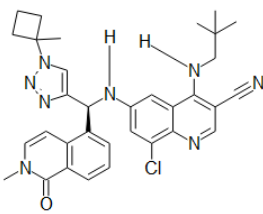
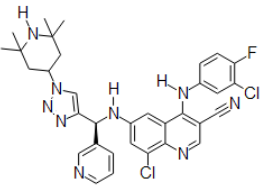
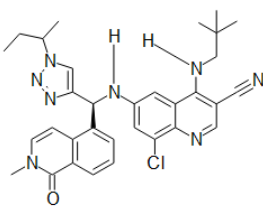
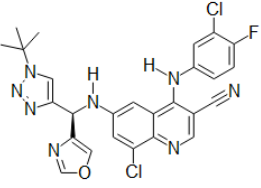
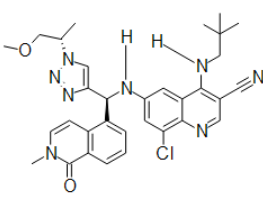
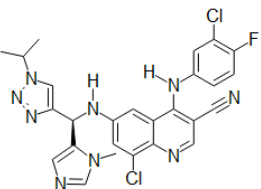
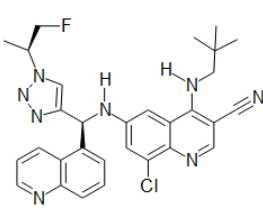
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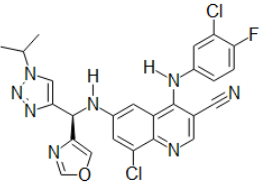
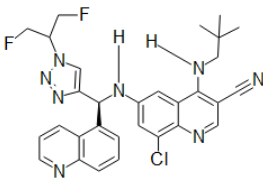
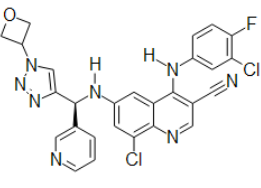
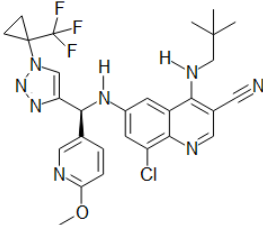
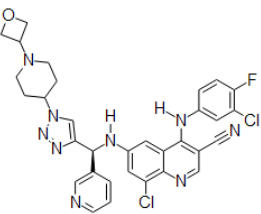
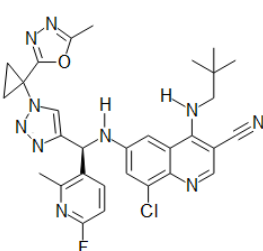
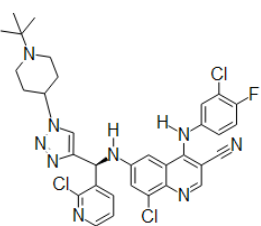
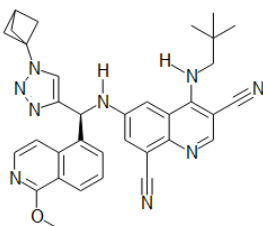
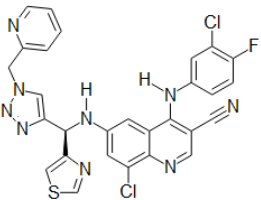
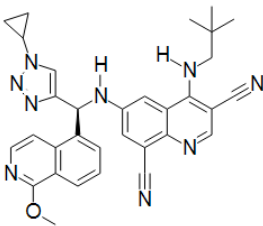
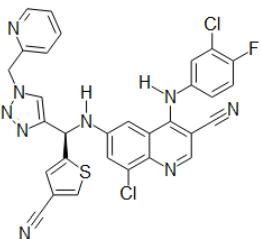
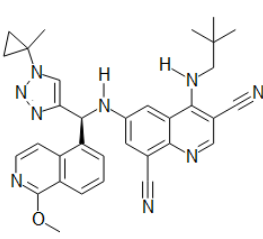
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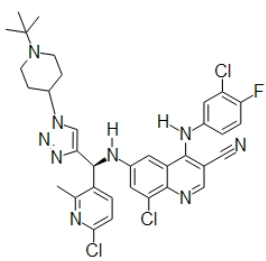
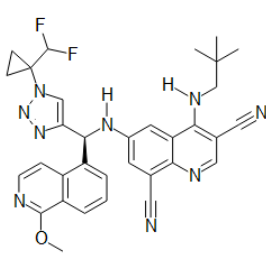
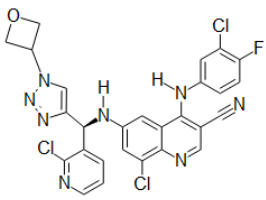
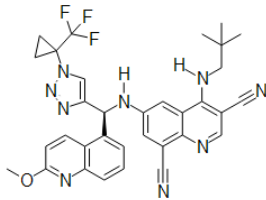
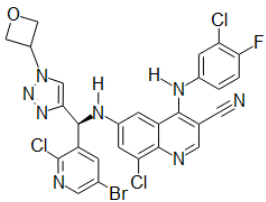
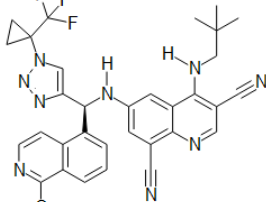
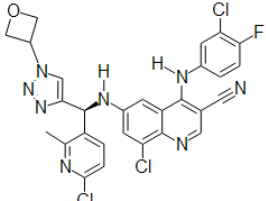
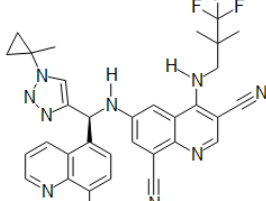
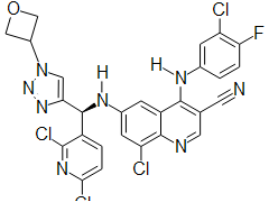
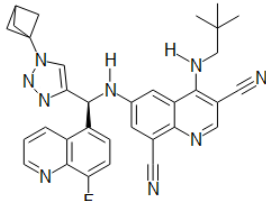
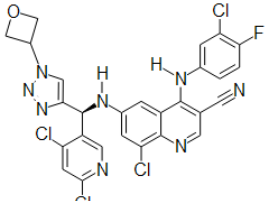
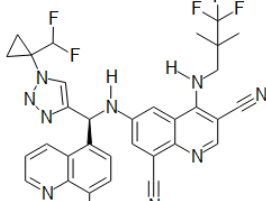
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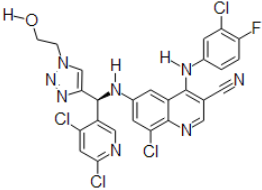
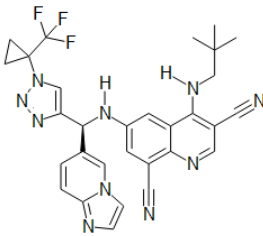
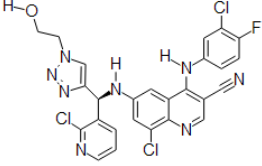
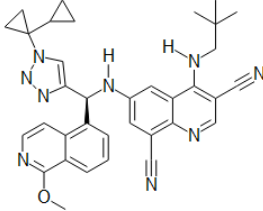
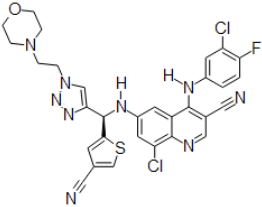
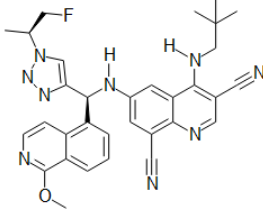
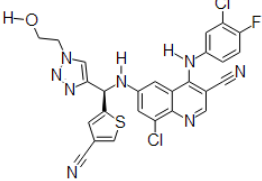
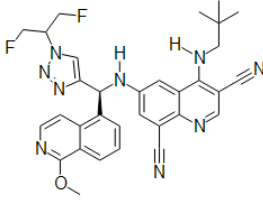
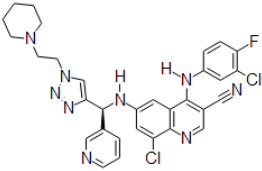
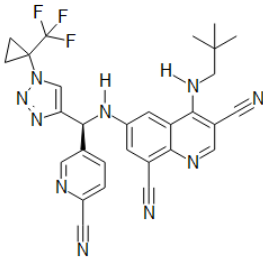
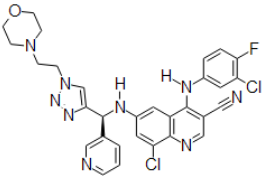
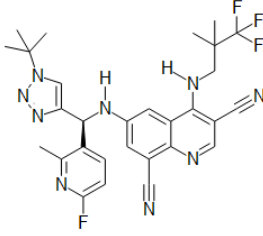
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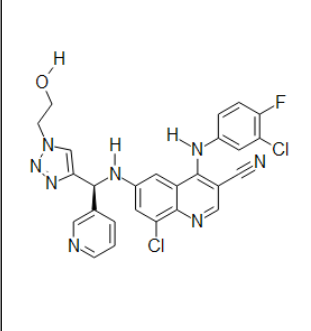
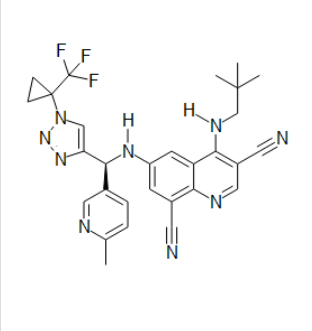
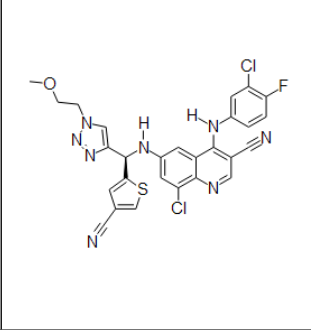
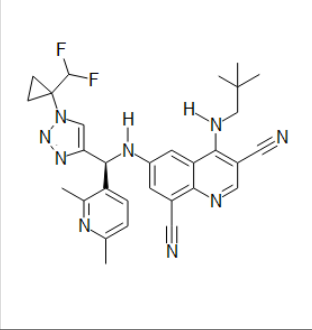
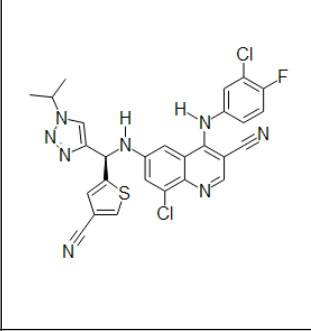
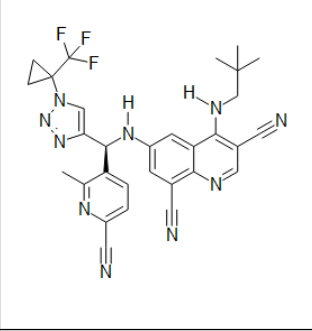
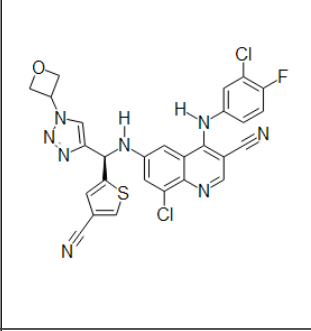
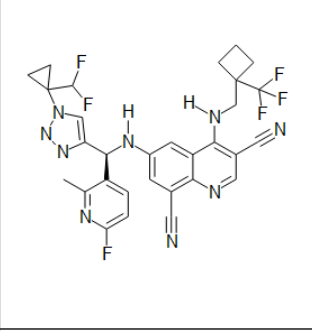
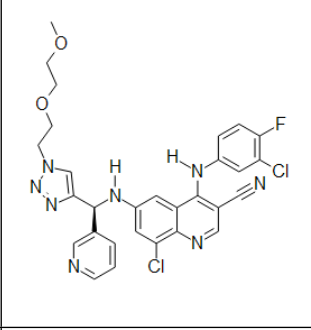
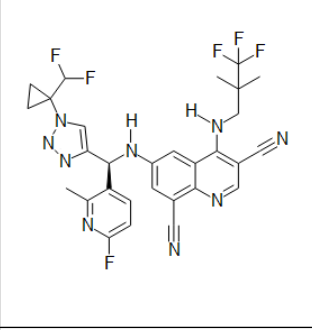
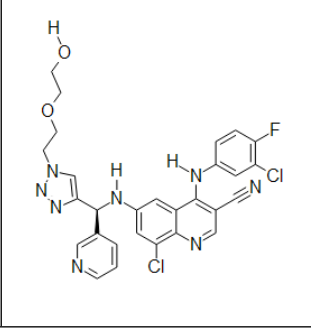
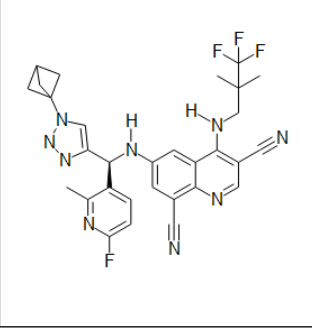
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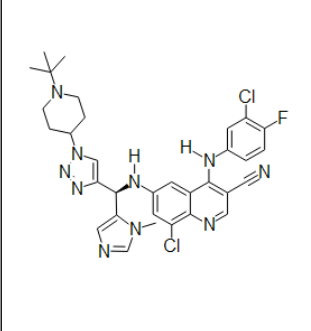
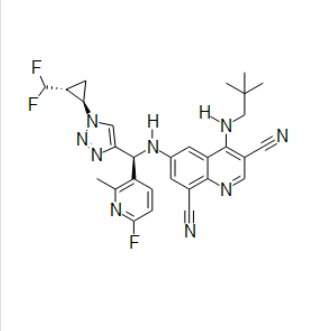
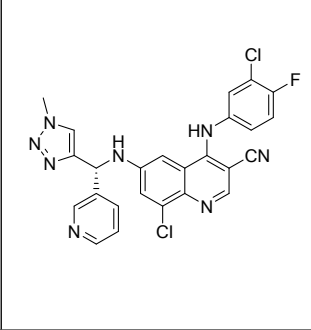
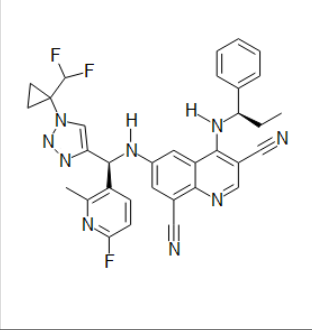
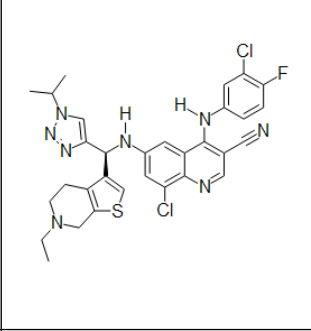
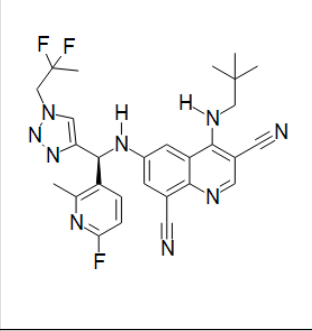
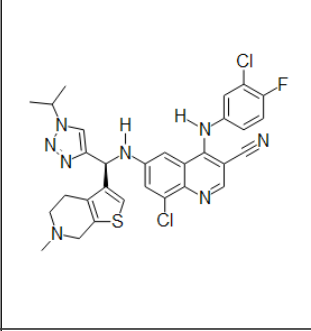
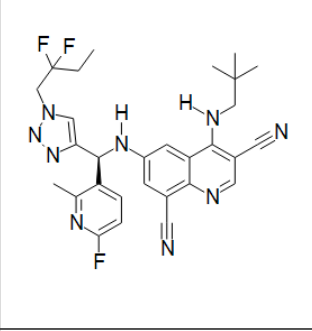
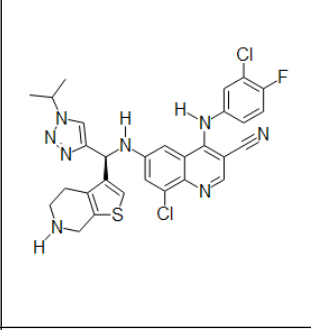
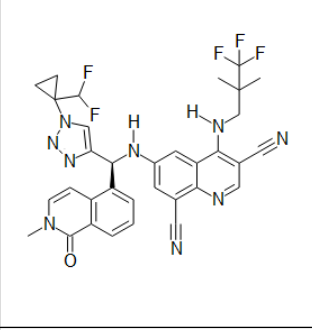
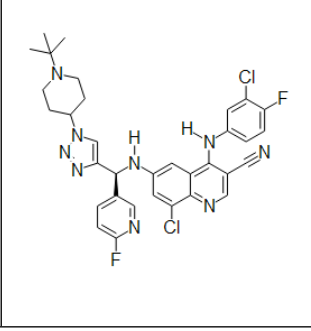
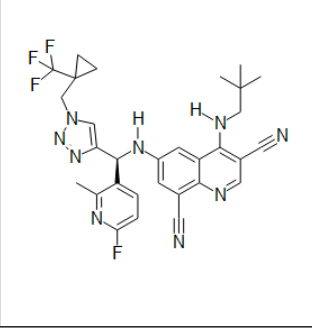
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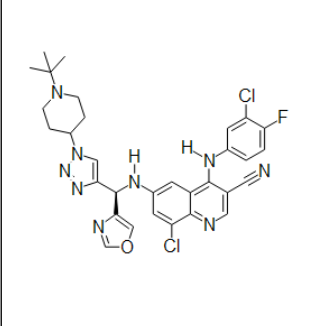
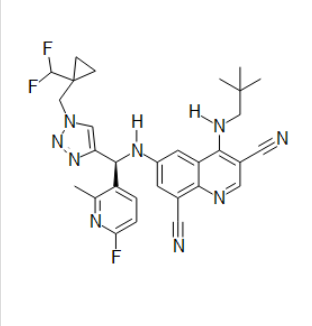
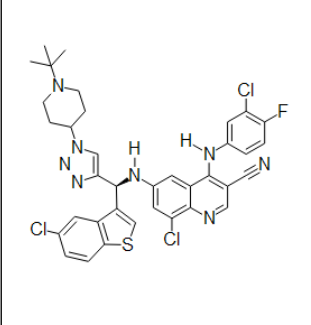
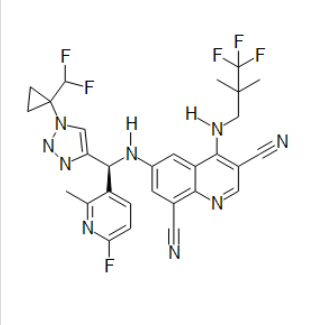
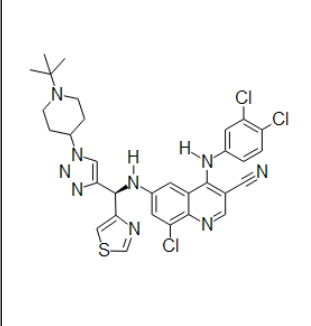
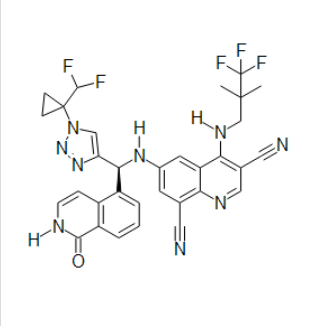
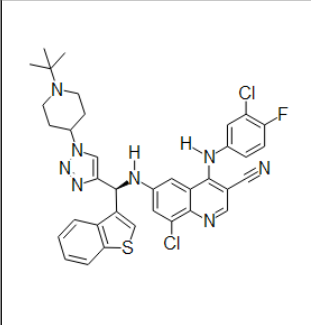
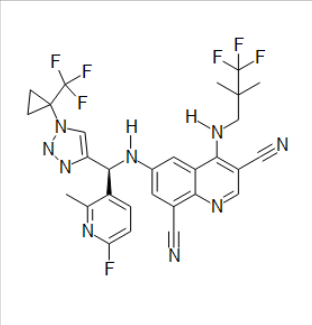
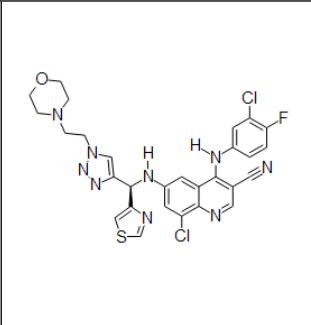
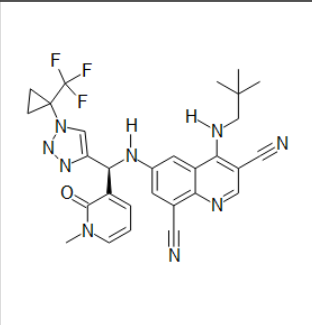
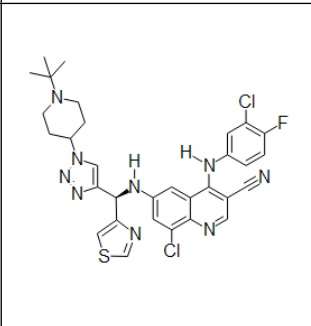
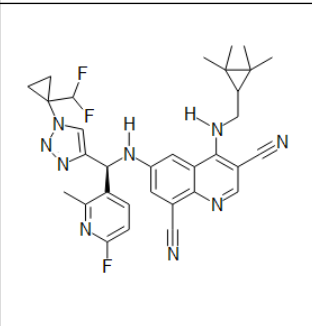
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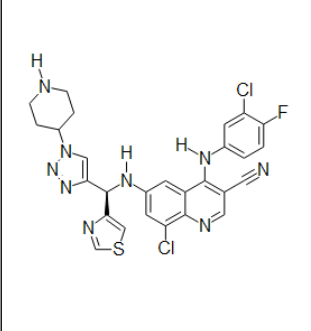
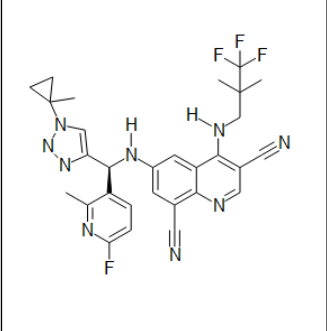
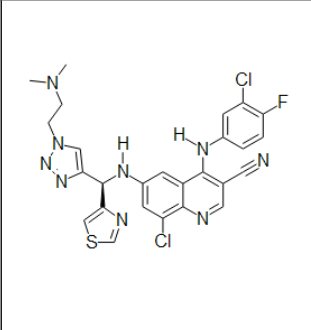
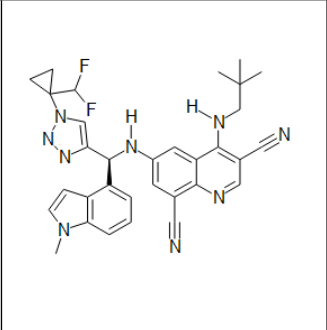
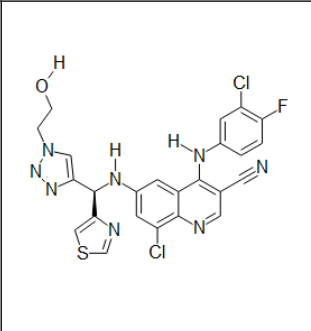
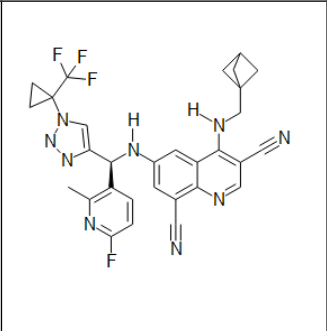
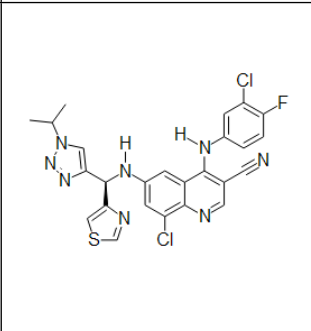
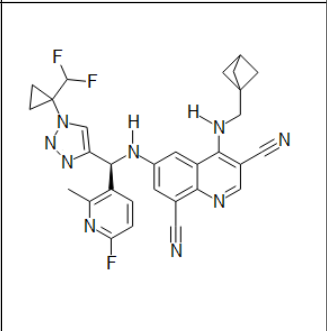
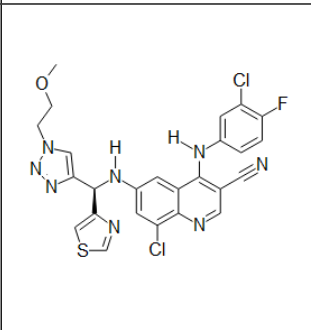
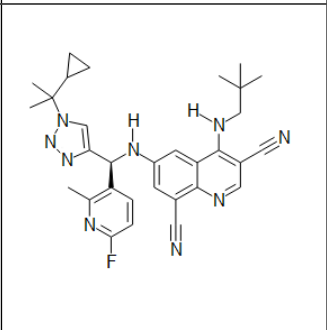
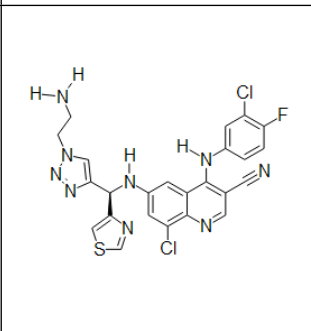
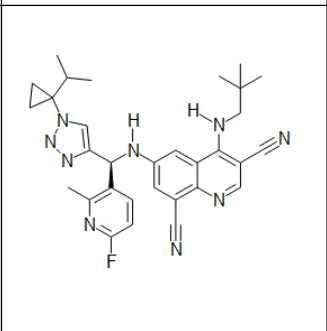
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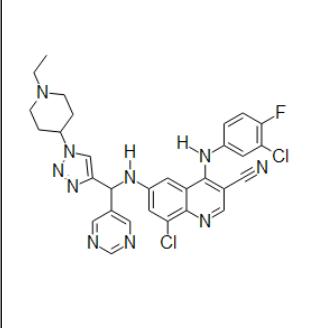
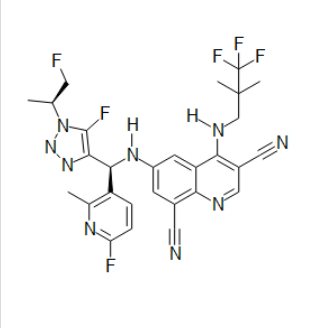
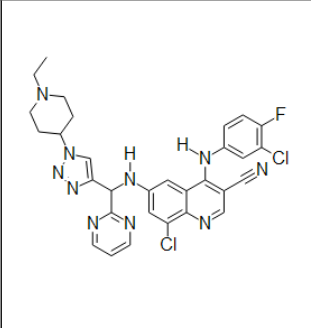
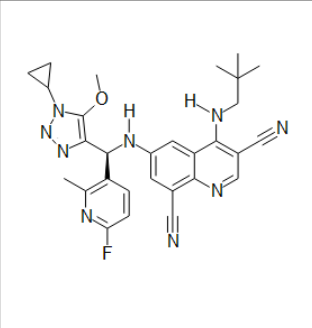
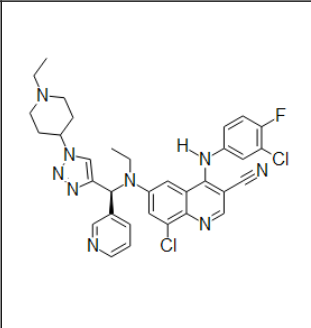
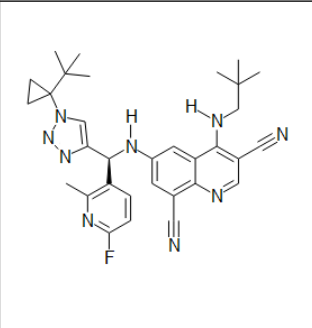
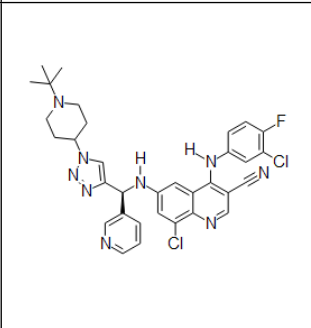
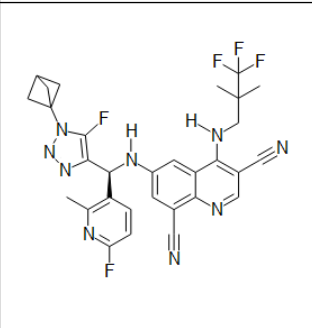
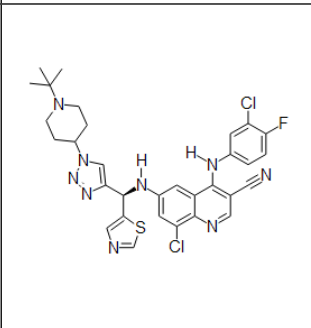
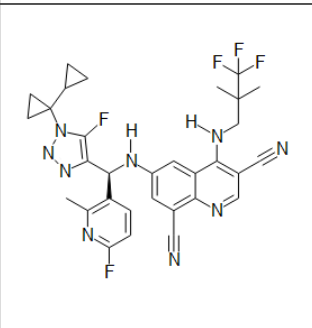
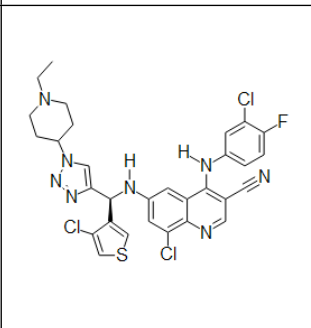
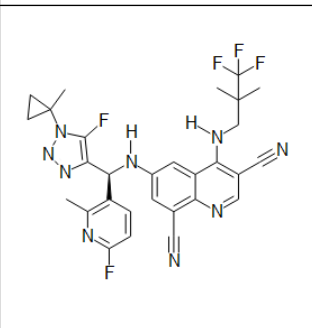
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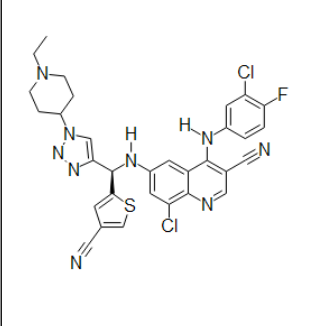
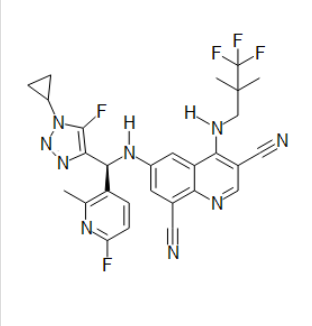
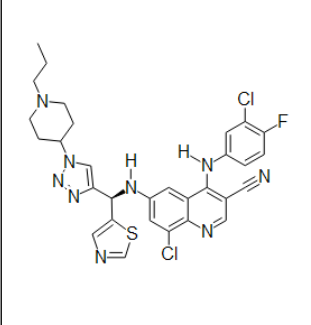
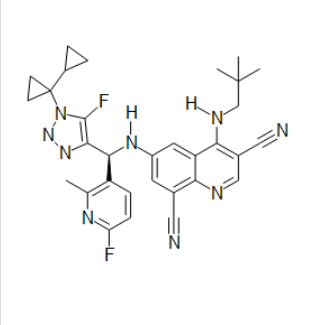
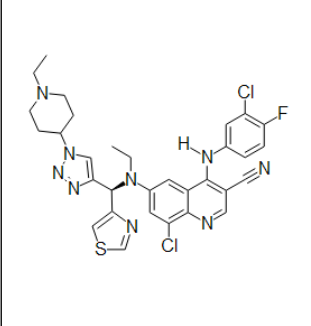
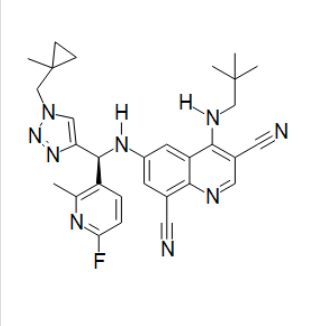
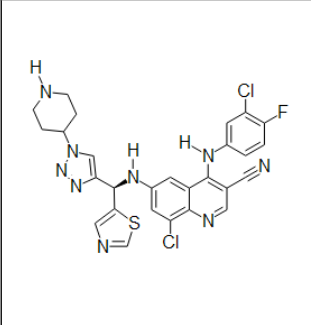
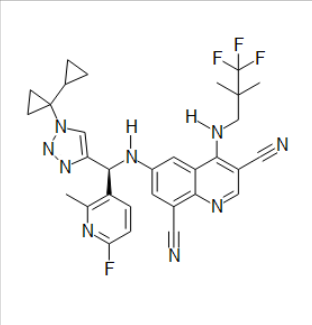
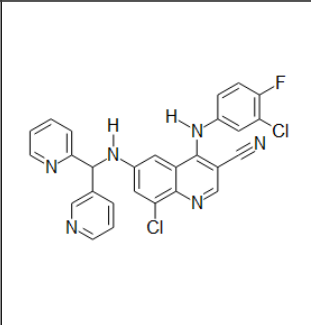
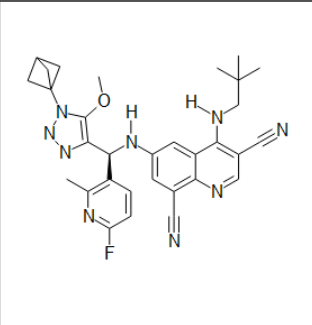
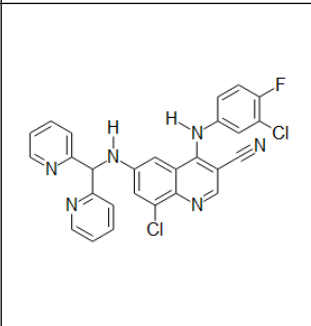
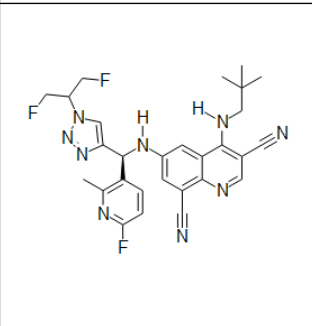
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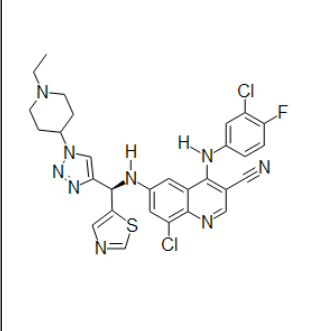
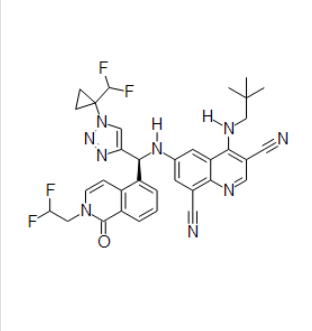
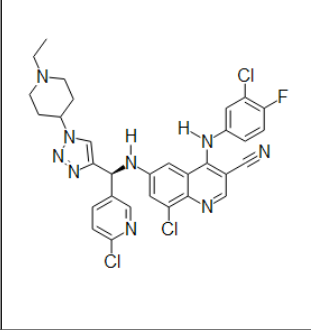
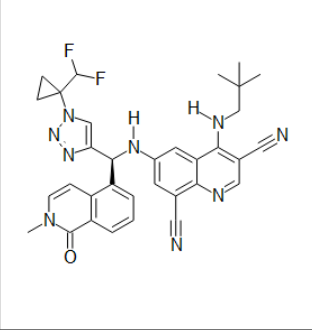
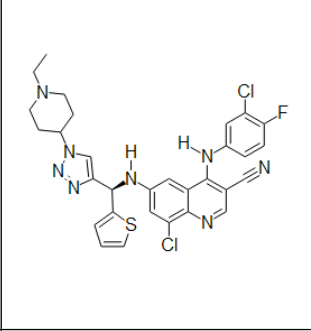
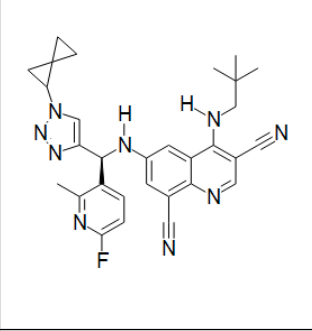
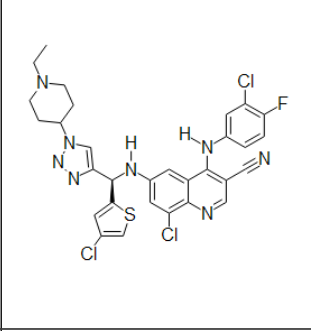
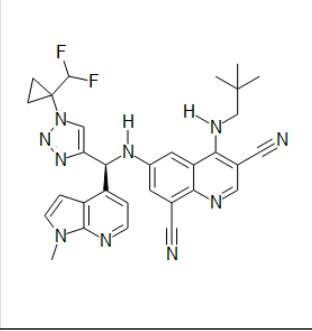
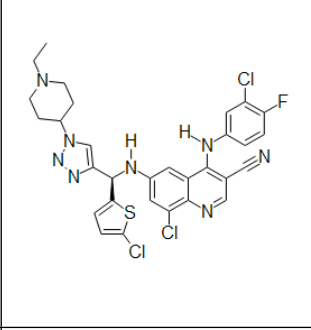
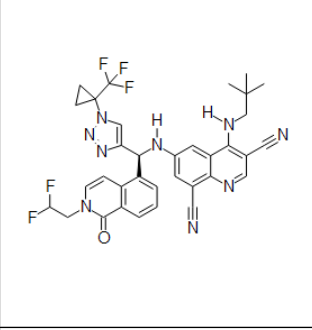
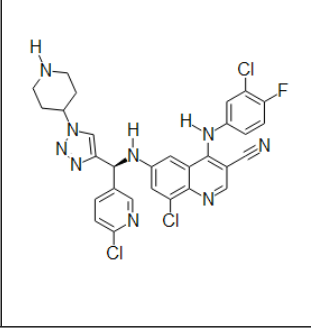
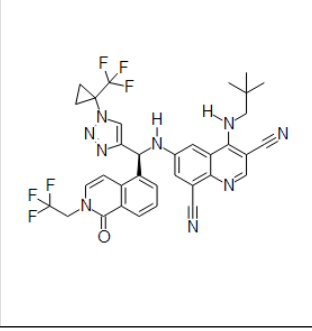
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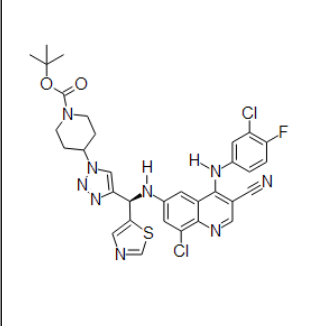
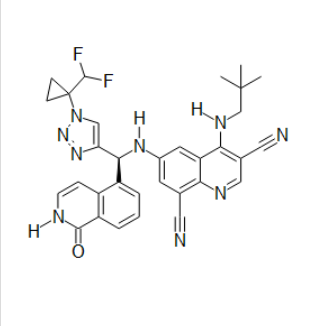
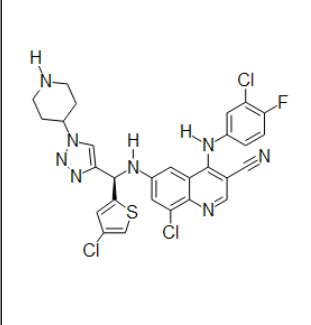
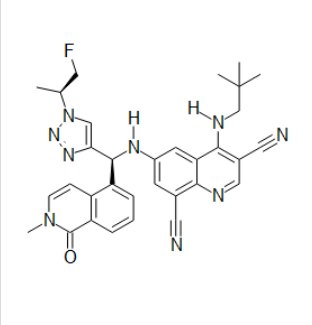
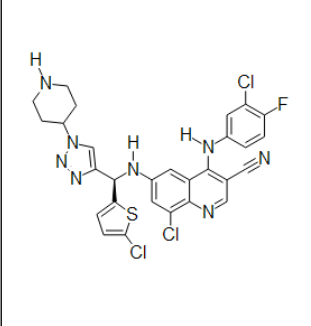
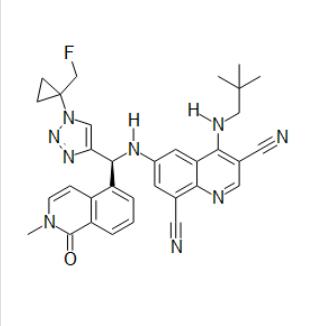
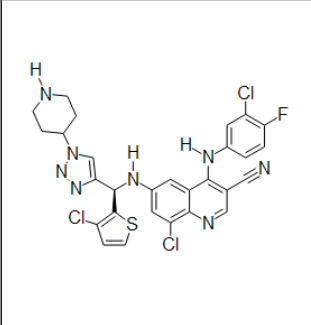
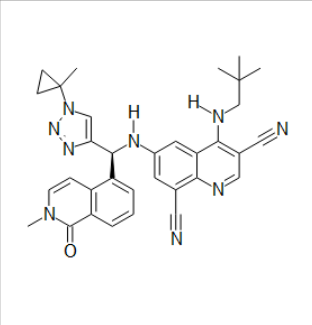
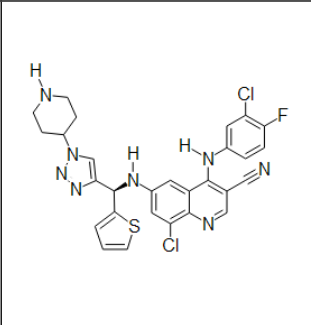
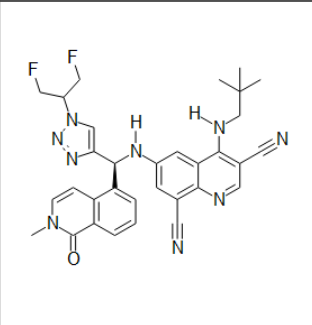
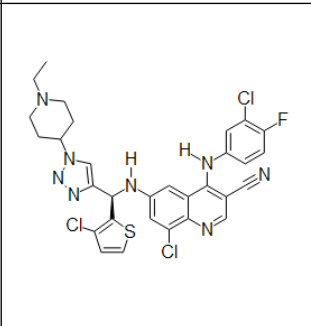
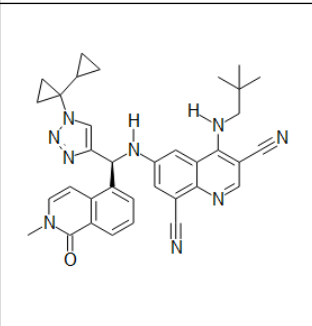
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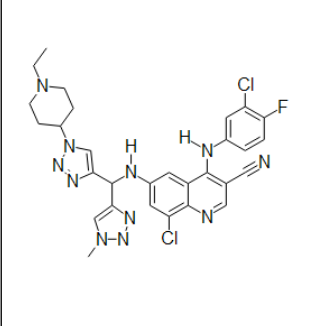
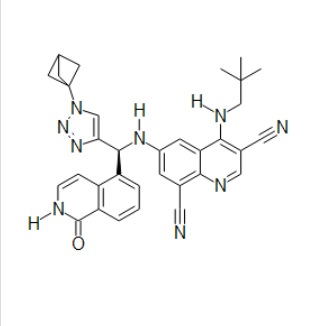
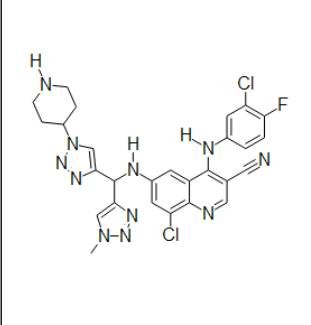
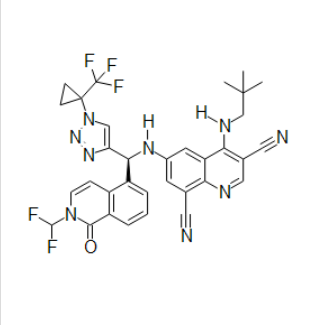
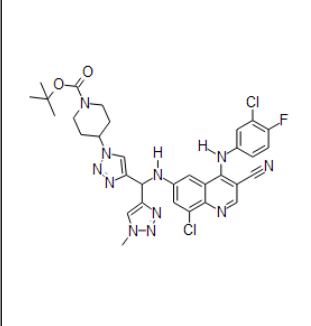
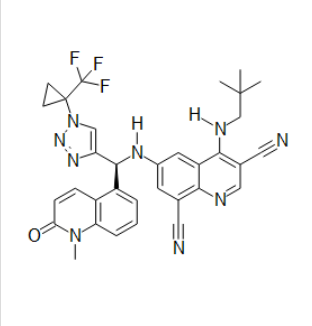
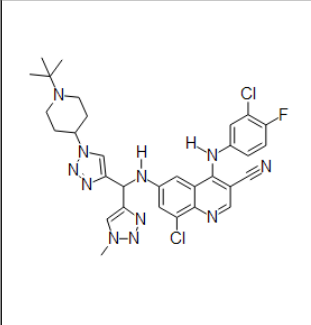
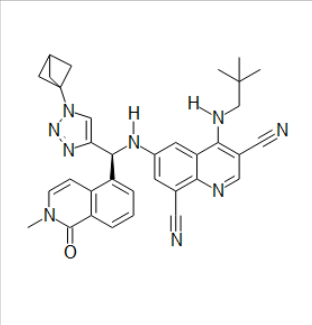
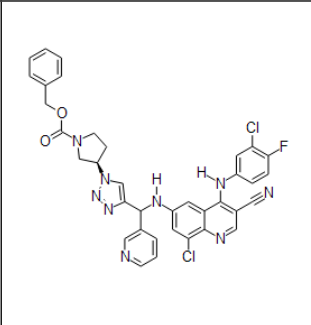
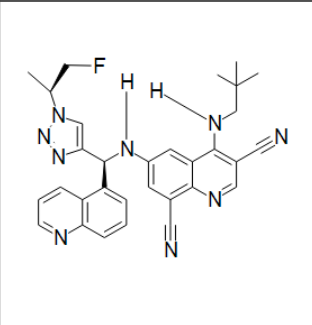
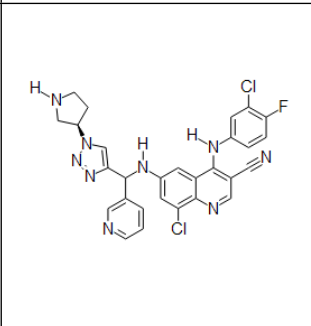
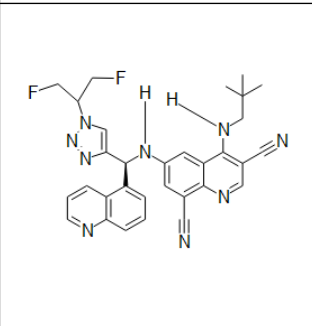
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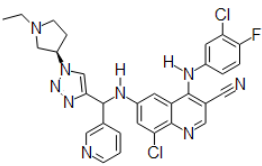
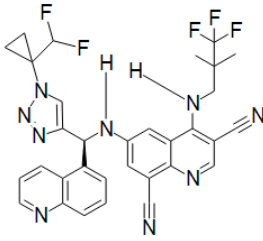
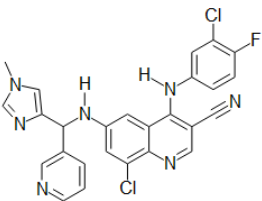
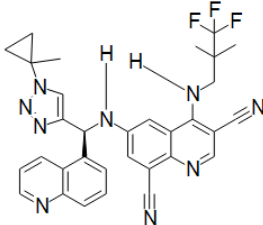
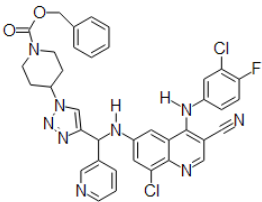
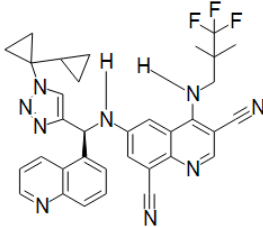
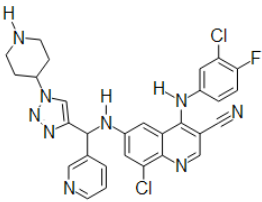
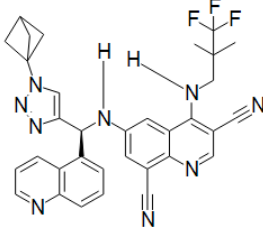
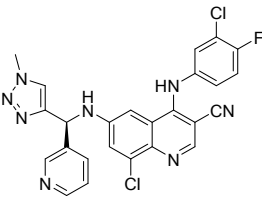
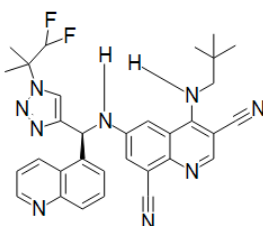
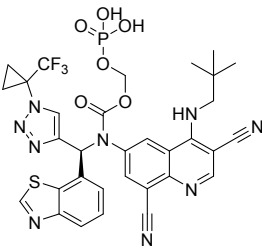
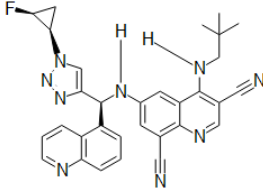
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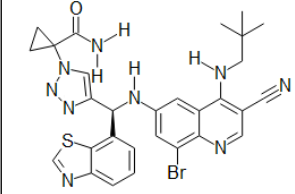
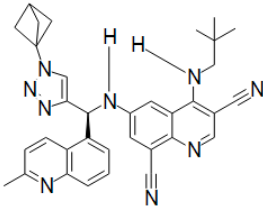
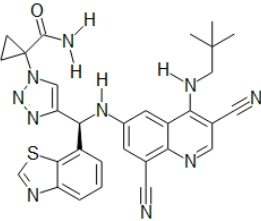
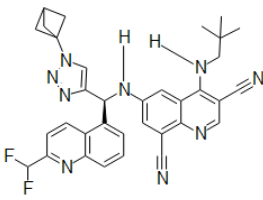
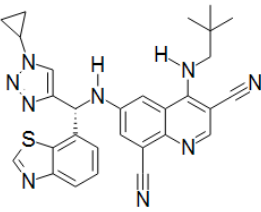
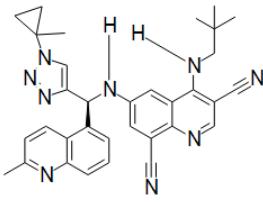
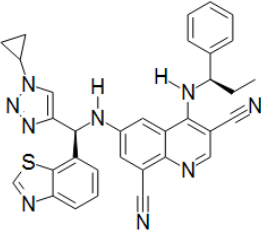
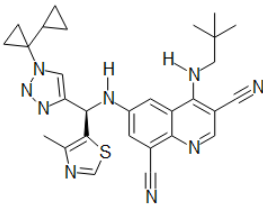
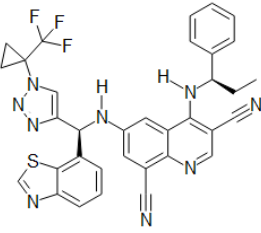
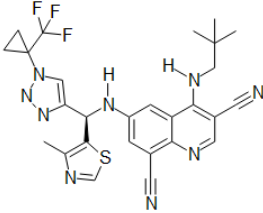
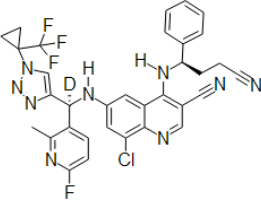
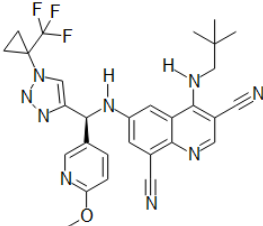
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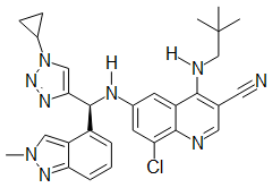
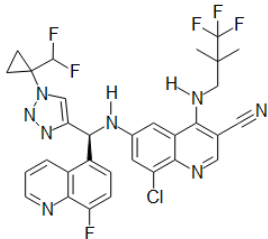
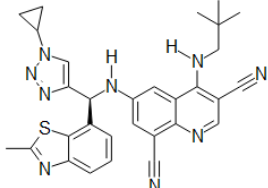
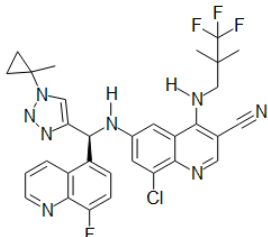
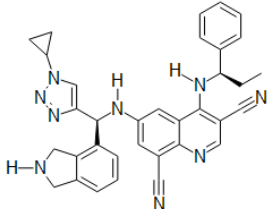
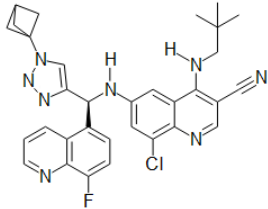
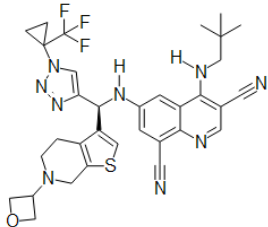
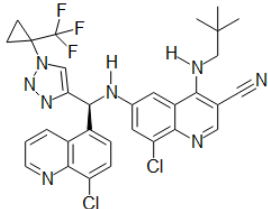
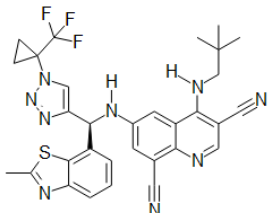
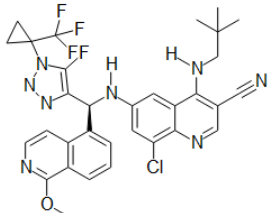
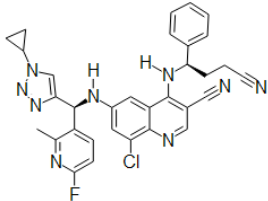
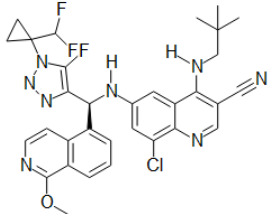
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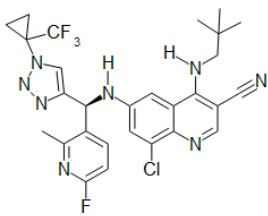
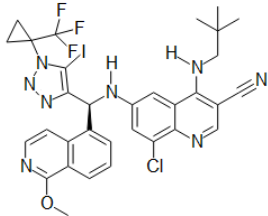
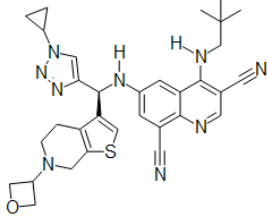
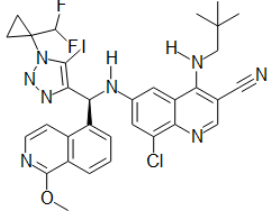
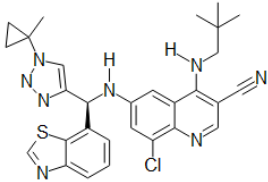
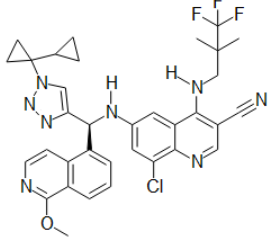
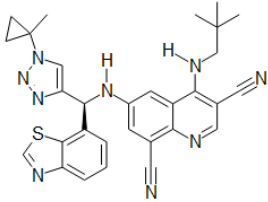
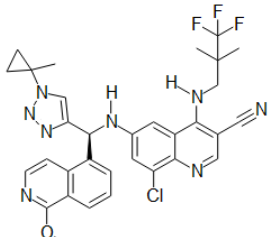
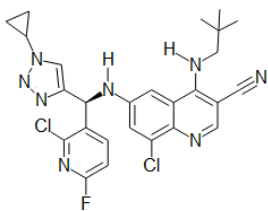
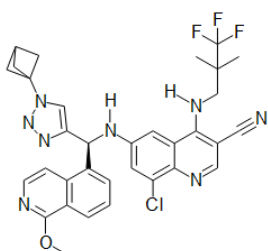
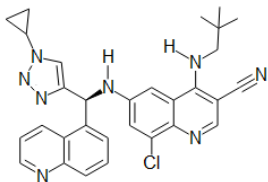
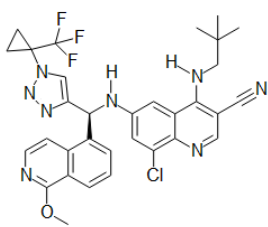
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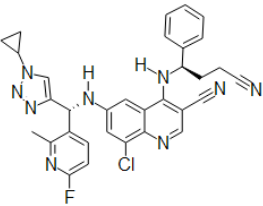
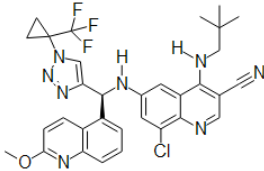
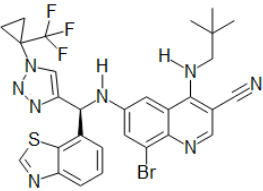
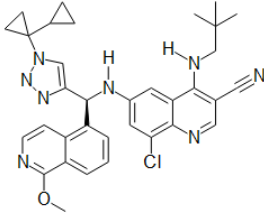
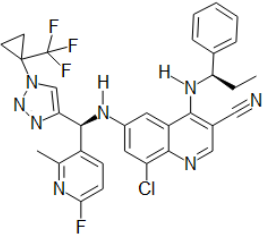
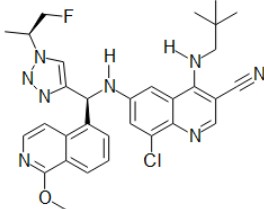
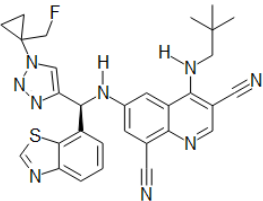
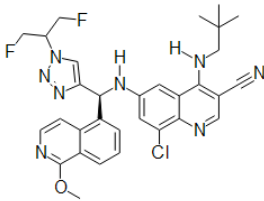
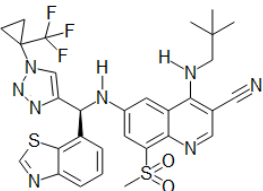
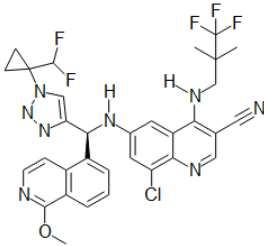
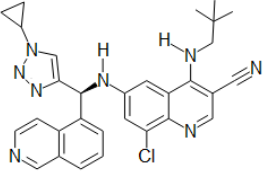
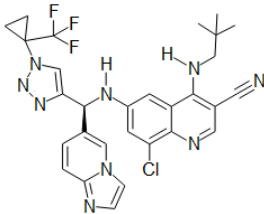
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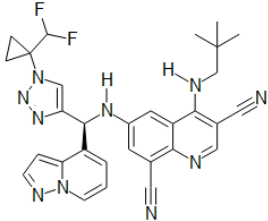
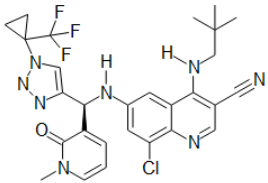
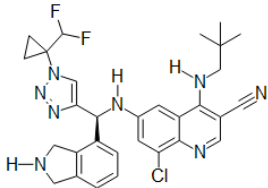
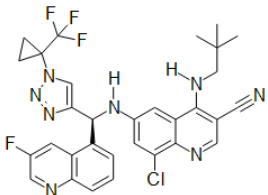
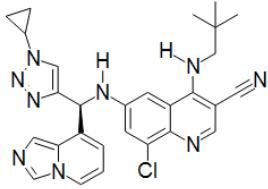
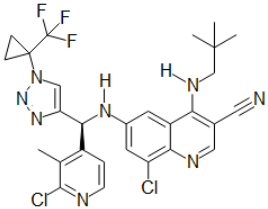
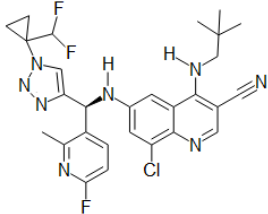
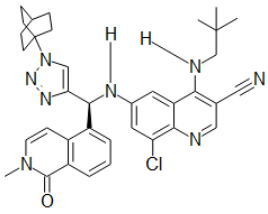
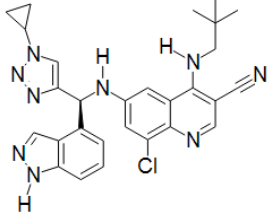
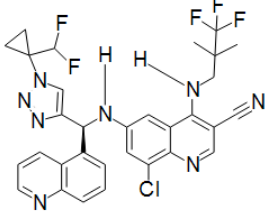
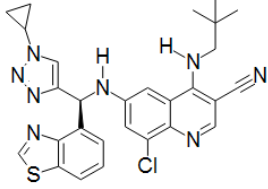
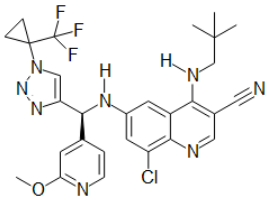
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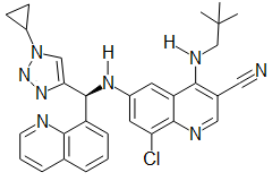
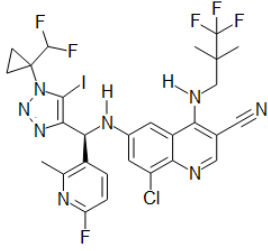
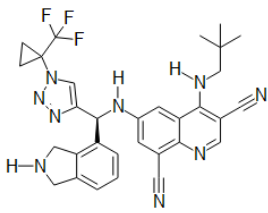
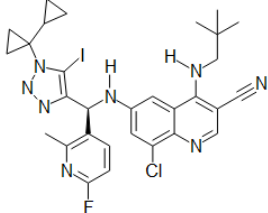
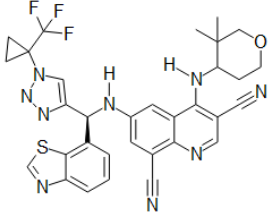
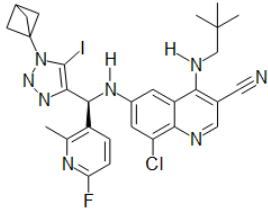
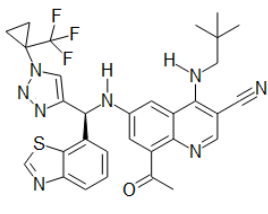
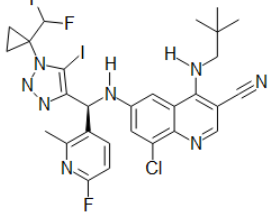
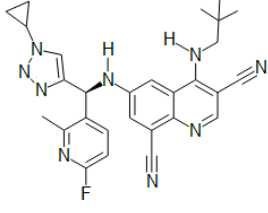
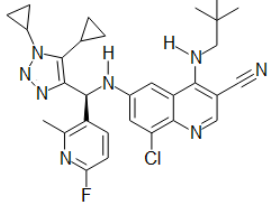
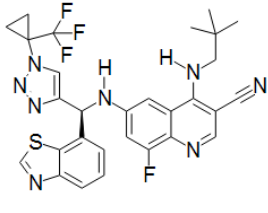
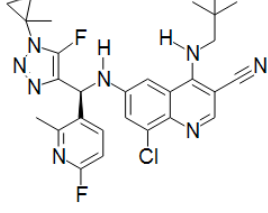
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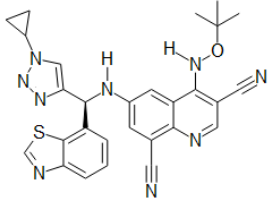
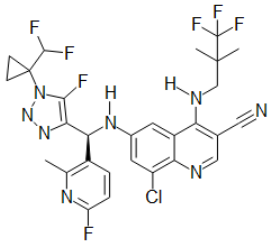
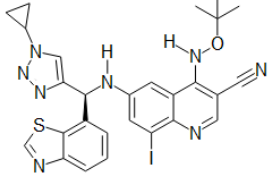
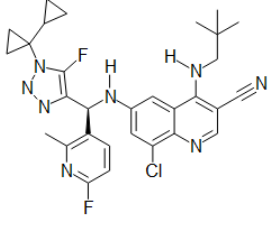
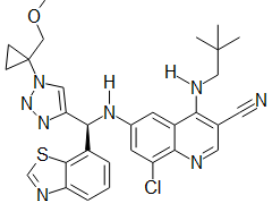
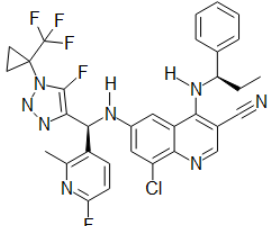
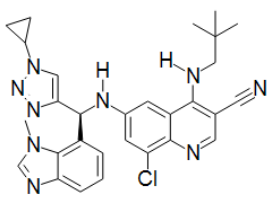
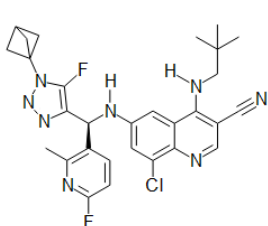
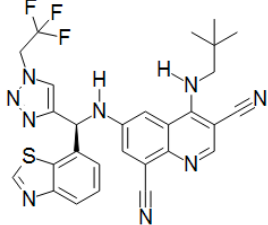
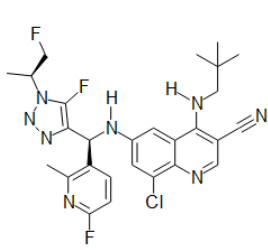
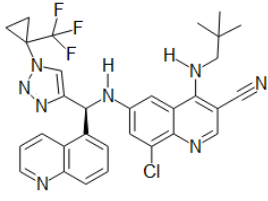
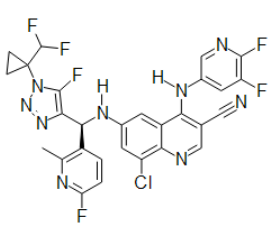
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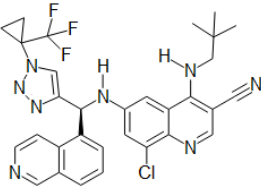
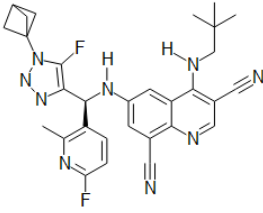
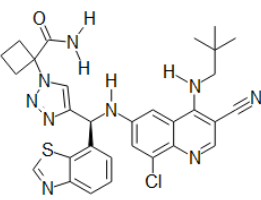
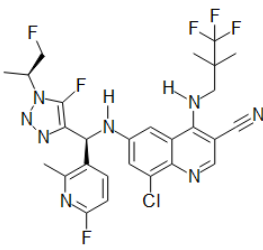
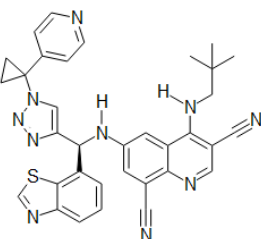
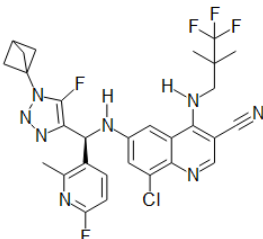
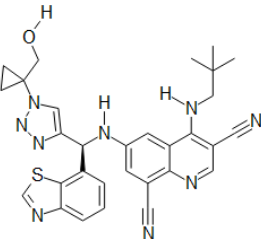
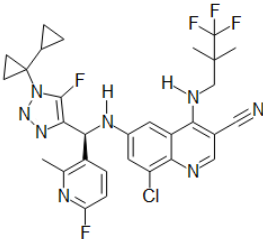
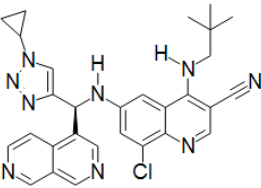
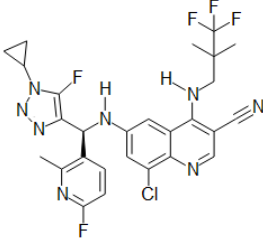
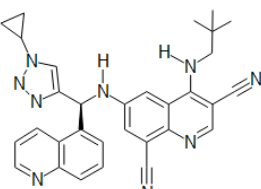
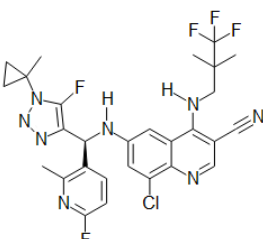
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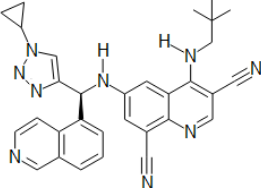
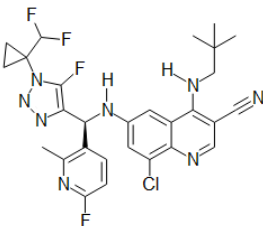
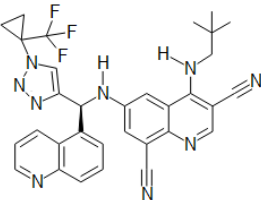
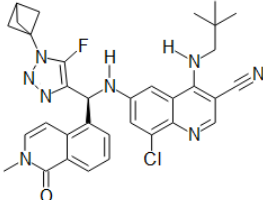
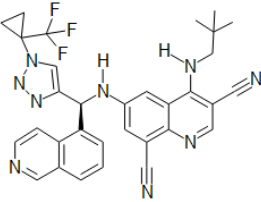
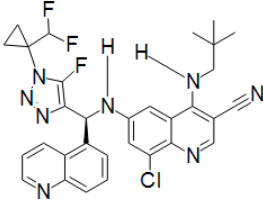
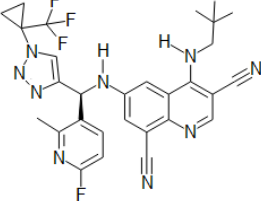
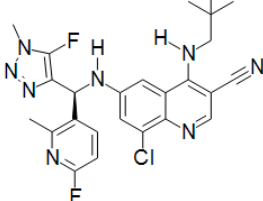
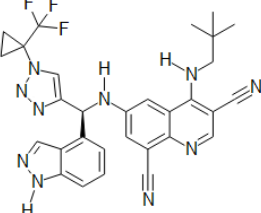
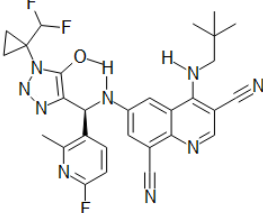
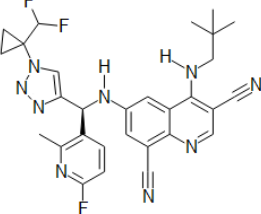
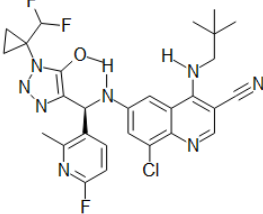
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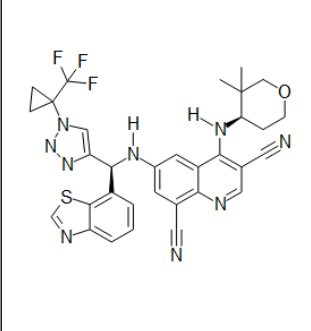
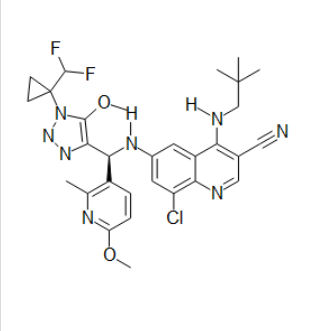
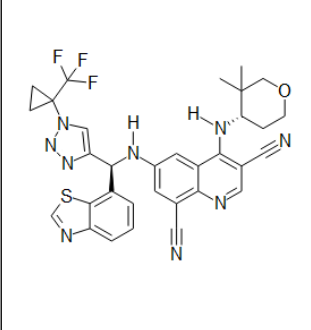
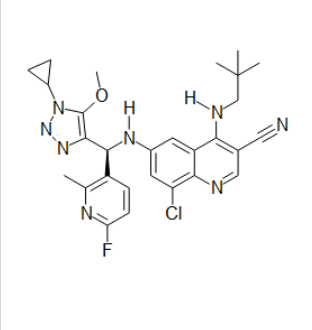
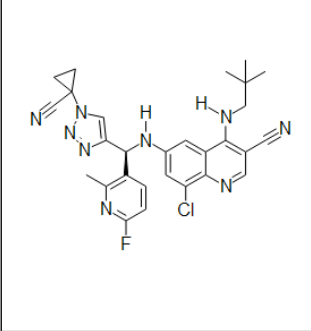
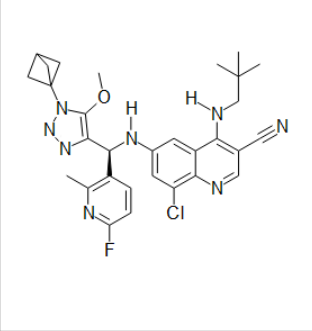
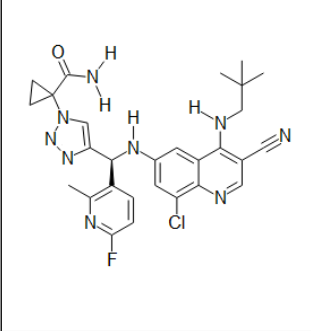
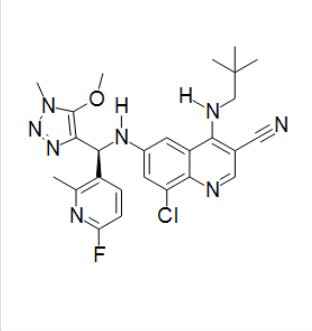
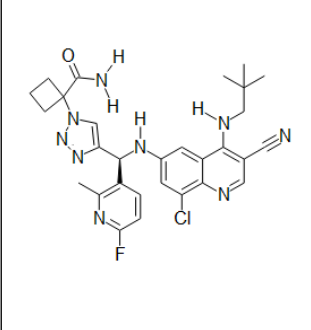
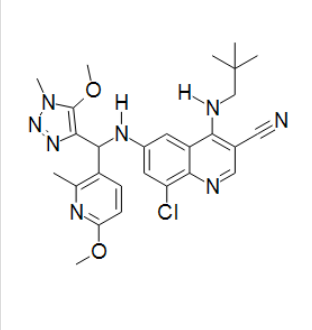
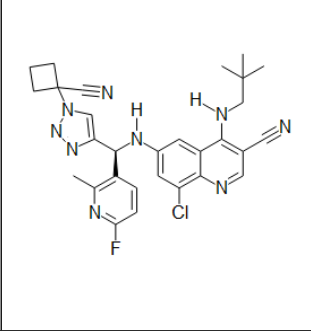
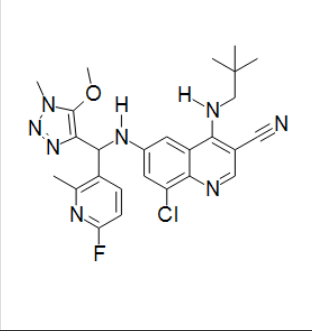
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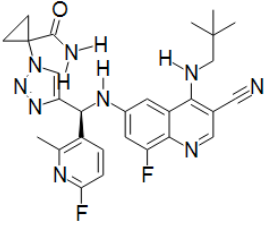
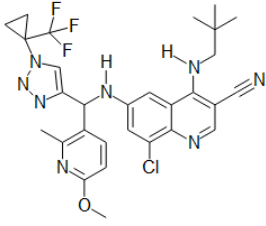
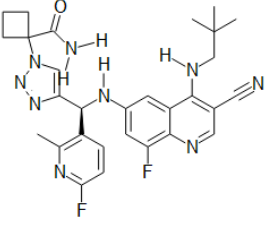
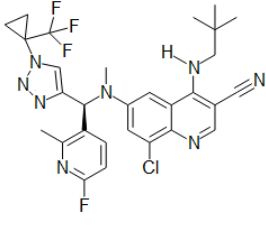
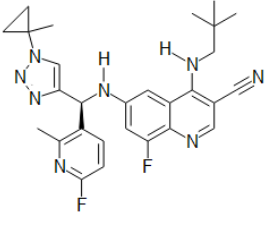
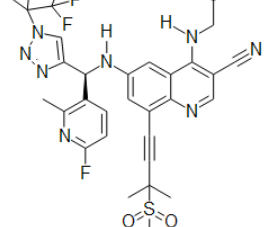
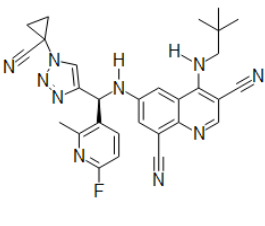
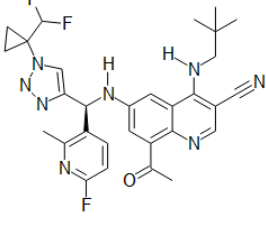
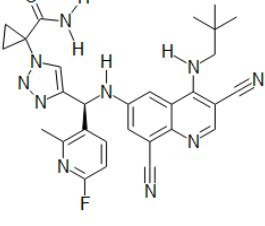
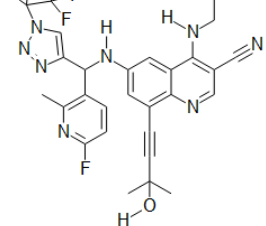
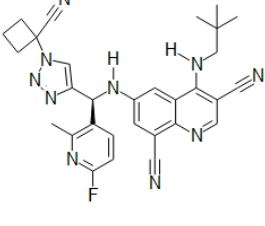
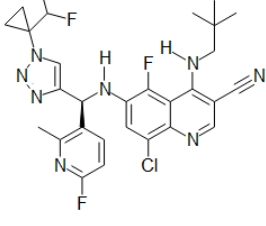
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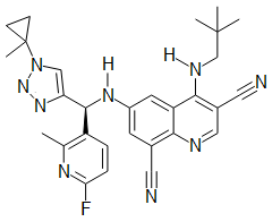
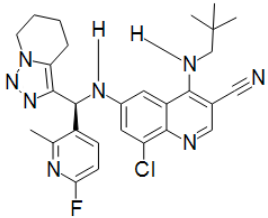
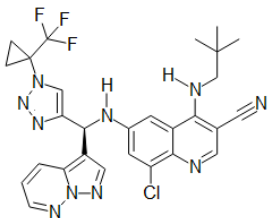
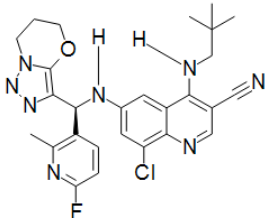
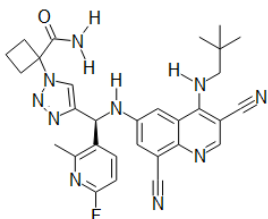
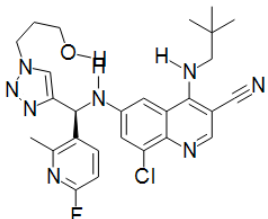
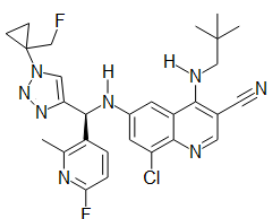
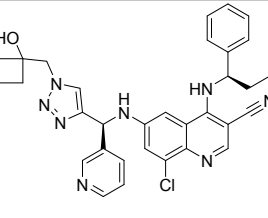
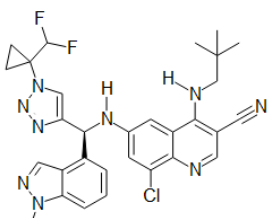
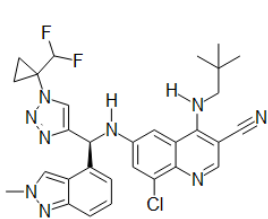
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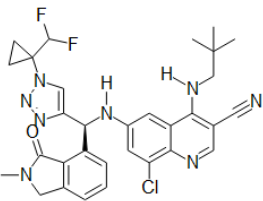
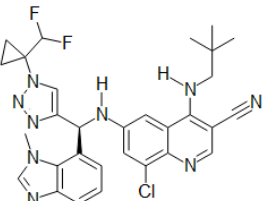
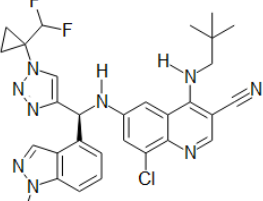
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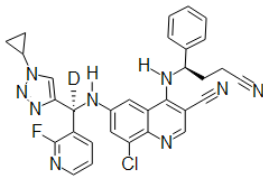
486		978	
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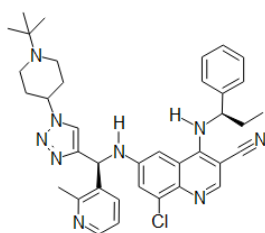
o una sal farmacéuticamente aceptable del mismo.

- 10. Una composición que comprende un compuesto de cualquiera de las reivindicaciones 1-9 y un vehículo farmacéuticamente aceptable.
- 11. El compuesto de la reivindicación 1, en donde el compuesto tiene la fórmula



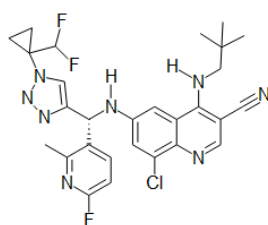
o una sal farmacéuticamente aceptable del mismo.

- 12. El compuesto de la reivindicación 1, en donde el compuesto tiene la fórmula



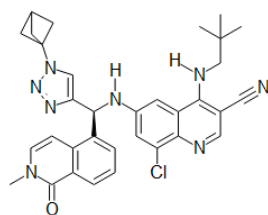
o una sal farmacéuticamente aceptable del mismo.

13. El compuesto de la reivindicación 1, en donde el compuesto tiene la fórmula



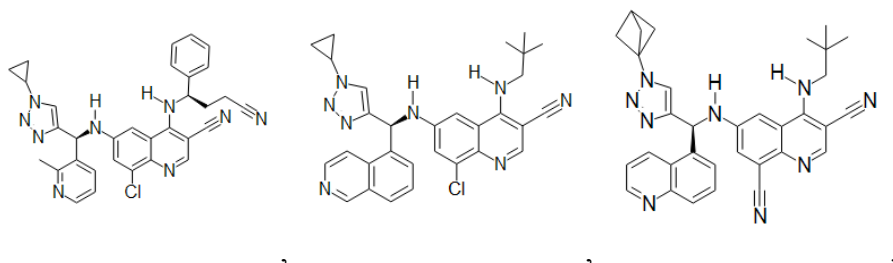
o una sal farmacéuticamente aceptable del mismo.

14. El compuesto de la reivindicación 1, en donde el compuesto tiene la fórmula



o una sal farmacéuticamente aceptable del mismo.

15. El compuesto de la reivindicación 1, en el que el compuesto tiene una de las siguientes fórmulas:



o una sal farmacéuticamente aceptable del mismo.

Señor
SUPERINTENDENTE DE INDUSTRIA Y COMERCIO
DIVISIÓN DE NUEVAS CREACIONES
E. _____ S. _____ D. _____

Trámite: 11
Evento: 378
Actuación: 444

Re: PI.-GILEAD SCIENCES, INC.-Solicitud de Patente de Invención en Fase Nacional PCT para "4,6-DIAMINOQUINOLINA-3-CARBONITRILOS SUSTITUIDOS PARA INHIBIR COT"-Clase C07D 401/14 número NC2017/0013351.

1. Me refiero al auto dictado por ese Despacho notificado por fijación en línea el 10 de diciembre de 2018.

2. Con el fin de responder las objeciones expuestas por la Señora Examinadora en su Concepto Técnico correspondiente al Oficio N° **14801** en relación con el título de la solicitud, y con la claridad y concisión del capítulo reivindicatorio, me permito dirigir su atención a las siguientes modificaciones y argumentos técnicos por medio de los cuales no sólo se superan completamente dichas objeciones sino que además se establece de manera incontrovertible la patentabilidad de la solicitud en estudio.

3. **TÍTULO.**

En relación con el título de la solicitud, la examinadora asegura que el título de la solicitud corresponde debe corresponder al objeto del mismo, y sugiere incluir la actividad como moduladores de la expresión o actividad de Cot de los compuestos reclamados.

Teniendo en cuenta la sugerencia de la examinadora, me permito manifestar que es deseo del solicitante modificar dicho título. De esta forma, el nuevo título se lee como sigue:

"4,6-DIAMINOQUINOLINA-3-CARBONITRILOS SUSTITUIDOS PARA INHIBIR COT"

En este sentido, me permito enfatizar que este nuevo título refleja de manera clara el objetivo de la invención, destacando las características técnicas esenciales de la materia reivindicada. Por lo tanto, el nuevo título cumple a cabalidad con la sugerencia presentada por la examinadora.

4. **CAPÍTULO REIVINDICATORIO.**

4.1. **Modificaciones al Capítulo Reivindicatorio.**

Me permito manifestar que es deseo del solicitante presentar un **capítulo reivindicatorio modificado**, que remplaza al actualmente presentado, con el propósito de superar las objeciones presentadas como parte del concepto técnico realizado por ese Despacho.

En conexión con el mencionado **capítulo reivindicatorio modificado**, me permito resaltar que éste no constituye de ninguna manera una ampliación al alcance de la solicitud, tal como fue originalmente presentada, toda vez que define claramente el objeto de la presente invención de acuerdo con las enseñanzas de la descripción. Dichas modificaciones se exponen a continuación:

- **La nueva reivindicación 1** corresponde a una nueva reivindicación independiente basada en la reivindicación 1 y 2(c) actualmente presentadas, en donde el término "*opcionalmente sustituido*" se cambió por "*sin sustituir o sustituido*".
- **Las nuevas reivindicaciones 2 a 9** se basan en las reivindicaciones 3 a 8 actualmente presentadas, en donde el término "*opcionalmente sustituido*" se cambió por "*sin sustituir o sustituido*".
- **La nueva reivindicación 9** se basa en la reivindicación 10 actualmente presentada, en donde la referencia a la tabla 1 ha sido eliminada y las estructuras de los compuestos de dicha tabla fueron colocados en la reivindicación.
- **La nueva reivindicación 10** corresponde a la reivindicación 11 actualmente presentada.
- **Las nuevas reivindicaciones 11 a 15** se basan en las reivindicaciones 12 a 16 actualmente presentadas, en donde ahora estas dependen únicamente de la nueva reivindicación 1.

De acuerdo a lo anterior, me permito señalar que **las reivindicaciones 1, 2 (puntos (a) y (b)), 17 y 18** del capítulo reivindicatorio actualmente presentado fueron **eliminadas**. Adicionalmente la numeración y dependencia fue modificada de acuerdo a las modificaciones previamente mencionadas.

De esta forma, **el capítulo reivindicatorio modificado queda constituido por 15 reivindicaciones**, las cuales se refieren de manera clara y concisa al objeto de la presente solicitud, y que cuenta con pleno sustento en las enseñanzas de la descripción.

4.2. Objeciones al Capítulo Reivindicatorio.

Ahora, la examinadora cuestionó la claridad y concisión del capítulo reivindicatorio con base en los siguientes comentarios:

- *"La reivindicación 1, no es clara al utilizar la expresión "opcionalmente sustituido" porque no es limitativa, además hace opcional la característica y no restringe el alcance de la reivindicación."*

Respecto a dicha objeción, me permito mencionar que la expresión objetada ha sido eliminada del capítulo reivindicatorio, y se ha reemplazado por la expresión "no sustituido o sustituido".

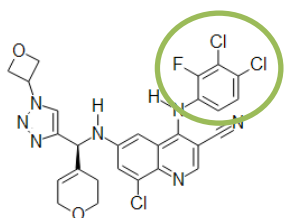
En consecuencia, amablemente solicito que la objeción a este respecto sea retirada.

- *"La reivindicación 1, presenta ilimitadas definiciones para los sustituyentes: R1,R2, R3,R4,R5,R6,R7,R8,R9,R10,R11,R12,R13,R14,R15, que a su vez pueden estar susutituidos por Z1,Z2,Z3,Z4,Z5,Z6,Z7,Z8,Z1a,Z1b, como por ejemplo: aril heteroaril, heterociclil opcionalmente sustituidos, que son géneros funcionales. Por lo tanto, se sugiere restringir la solicitud a una razonable generalización del tipo de compuestos que han sido sintetizados ó probados, es decir, que se encuentran debidamente sustentados, conforme a la siguiente tabla."*

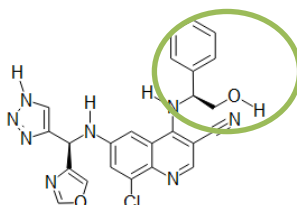
En este caso, me permito indicar que el capítulo reivindicatorio ha sido modificado para restringir la materia a reclamar. En este sentido, por favor note que la estructura Markush se basa ahora en la Fórmula IIIA la cual tiene un alcance más limitado que la Fórmula I actualmente reclamada. Por lo tanto, la persona normalmente versada en la materia determinaría sin problema alguno los compuestos derivados de la Fórmula IIA.

Adicionalmente, me permito mencionar que la tabla presentada por la examinadora claramente no refleja la diversidad de compuestos sintetizados y probados por el solicitante, a saber:

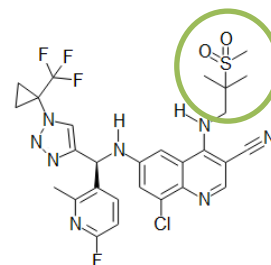
- La examinadora señala que R¹ es neopentil, fenil sustituido con ciano o propil, piridina sustituida con F, pirano sustituido con dimetil, adamantano, cicloheptil, ciclobutil, biciclohexano, y trifluoro-2,2-dimetilpropil; sin embargo, los ejemplos muestran otros sustituyentes como por ejemplo (circulo verde):



Compuesto 210

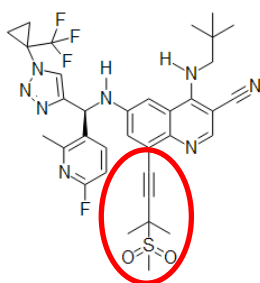


Compuesto 215

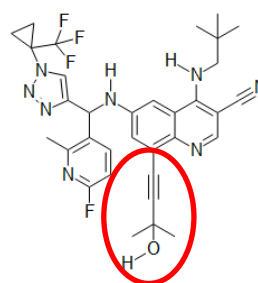


Compuesto 722

- La examinadora indica que R⁵ es solo Cl, CN, Br y metoxi, sin embargo, a modo de ejemplo, los compuestos 980 y 982 tiene a diferente grupo en esa posición (círculo rojo):



Compuesto 980



Compuesto 982

A la luz de lo anterior, es claro que el capítulo reivindicatorio modificado refleja los compuestos sintetizados junto con todos los posibles sustituyentes que se pueden encontrar en los 987 compuestos ejemplificados en la descripción.

Por lo tanto, amablemente solicito que la objeción a este respecto sea dada por superada.

- “En la reivindicación 9, se sugiere definir de cuál reivindicación depende específicamente.”

A este respecto, me permito indicar que la nueva reivindicación 8 (reivindicación 9 actualmente presentada) ha sido modificada para ser dependiente de la nueva reivindicación 1. En este sentido, respetuosamente solicito que la objeción sea superada.

- “La reivindicación 10 hace referencia a la descripción (Tabla 1). Las reivindicaciones no deben contener tales referencias y deben ser claras por sí mismas.”

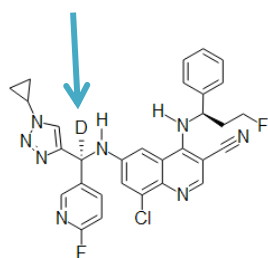
Frente a esta objeción, me permito llamar la atención sobre las modificaciones al capítulo reivindicatorio, en donde se han adicionado los compuestos de la tabla 1 en la nueva reivindicación 9 (reivindicación 10 actualmente presentada) y, por lo tanto, la referencia a dicha tabla 10 ha sido eliminada. De acuerdo a lo anterior, la objeción mencionada ha sido completamente superada.

- “Las reivindicaciones 12 a 16 reclaman un compuesto y la hacen dependiente de la reivindicación 11 que es de composición. Se sugiere hacer la dependencia de manera correcta.”

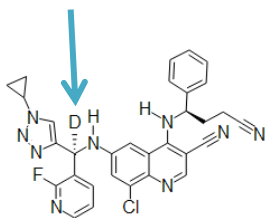
Con respecto a esta objeción, me permito aclarar que las nuevas reivindicaciones 11 a 15 (reivindicaciones 12 a 16 actualmente presentadas) se han modificado para depender solamente de la nueva reivindicación 1. En consecuencia, la objeción mencionada ha sido superada completamente.

- “La expresión “análogo deuterado”, mencionada específicamente en las reivindicaciones 1, 2, 5, y sus dependientes, hace que el alcance no sea claro ya que no se sabe a qué estructuras se refiere porque incluye un número ilimitado de compuestos que se pueden obtener de otro compuesto por alguna modificación química indeterminada. De manera que, no es claro cuales compuestos quedan comprendidos dentro del alcance de las reivindicaciones y cuáles no.”

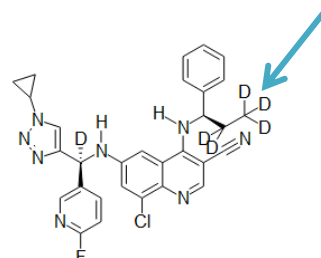
A este respecto, nos encontramos en desacuerdo con la opinión de la examinadora ya que varios ejemplos en la descripción que muestran análogos deuterados de los compuestos reclamados, como por ejemplo:



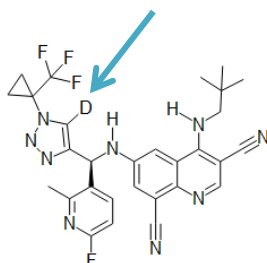
Compuesto 11



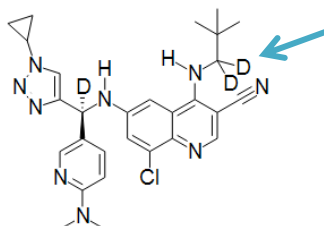
Compuesto 71



Compuesto 106



Compuesto 679



Compuesto 711

Del mismo modo, me permito aclarar que la persona normalmente versada en la técnica sabe fácilmente cómo obtener un análogo deuterado de cualquiera de los compuestos reivindicados, ya que el intercambio de hidrógeno por deuterio es ampliamente conocido en el estado de arte.

En consecuencia, solicito amablemente que la objeción sea reconsiderada.

- *“Las reivindicaciones 2(a) y 4 no son claras al utilizar la disyunción “y/o”, cuando se escoge la opción “o” dado que R2 y m, tienen diversos significados; así como, W, X, Y y Z3 contemplan diferentes significados.”*

En relación con esta objeción, me permito mencionar en primer lugar que la reivindicación 2(a) ha sido eliminada. Ahora, con respecto a la actual reivindicación 4 (nueva reivindicación 3), está perfectamente claro que cualquier persona versada en la técnica, incluso cualquier persona, puede entender cuál es el significado de “y/o”, que es la forma de unir una conjunción copulativo y disyuntiva.

En el caso de la presente invención, teniendo en cuenta que la nueva reivindicación 3 es una realización preferida de los compuestos reivindicados en la nueva reivindicación 1, entonces el significado de “y/o” es que puede tener ambas condiciones (1) y (2) en la realización, o puede tener solo uno de ellos.

A la luz de lo anterior, me permito enfatizar que la nueva reivindicación 3 es completamente clara y, por lo tanto, la anterior objeción ha sido superada.

- *“En la reivindicación 18 se reclama una composición que comprende un compuesto o composición de acuerdo a cualquiera de las reivindicaciones 1-17 y un agente antiinflamatorio adicional. Sin embargo, en el desarrollo de la invención de acuerdo con la descripción no se observa la obtención de este tipo de composiciones con dos o más principios activos, en consecuencia no existe evidencia del efecto que están puedan generar.”*

La anterior objeción ha sido completamente superada ya que la reivindicación 18 ha sido eliminada del capítulo reivindicatorio modificado que se presenta junto al presente memorial.

En vista de dichas modificaciones, me permito resaltar que el capítulo reivindicatorio modificado es totalmente claro y conciso al reclamar los compuestos 6-diaminoquinolina-3-carbonitrilos sustituidos para inhibir COT, dado que define la invención a través de sus características técnicas esenciales. Asimismo, dicho capítulo modificado supera completamente las objeciones de claridad presentadas por la señora examinadora y, por ende, cumple a cabalidad con lo estipulado por el Artículo 30 de la Decisión Andina 486 de 2000.

5. **CONCLUSIÓN.**

Para finalizar, me permito reiterar que el capítulo reivindicatorio modificado, presentado junto con el presente memorial es totalmente claro, conciso y cuenta con pleno soporte en la descripción al reclamar el reclamar los compuestos 6-

diaminoquinolina-3-carbonitrilos sustituidos para inhibir COT, cumpliendo así con lo exigido por la mencionada Decisión Andina 486 de 2000.

Por otro lado, me permito mencionar que el objeto de la solicitud en estudio, es novedoso y de ninguna manera resultaría evidente para la persona normalmente versada en la materia a partir de las enseñanzas del estado arte previo, demostrando irrefutablemente la patentabilidad de la presente solicitud.

6. Anexo al presente memorial, me permito presentar una copia de:

- Las **páginas 513 a 609** que corresponden al **capítulo reivindicatorio modificado**, tal como se discutió en el presente memorial, constituido por **15 reivindicaciones**.

7. En vista de lo anterior, ruego a usted proceder a estudiar nuevamente la solicitud a la luz de las modificaciones y los argumentos presentados y conceder el privilegio de patente solicitado.

Señor Superintendente,



ALICIA LLOREDA RICAURTE

T.P. 53.215

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notificacionespatentes@lloredacamacho.com