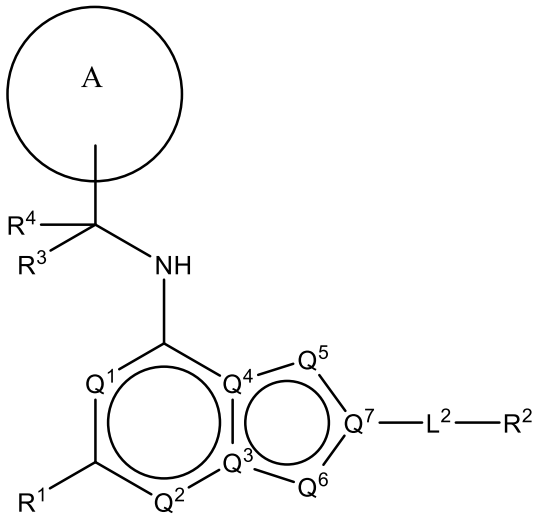
Natl. Acad. Sci. 2014, 111(9):3401-6). However, binding of these molecules seems to lead to increased nucleotide exchange and thereby activation of RAS instead of deactivation.

[0010] In an effort to stabilize the protein-protein-interaction of RAS-family proteins with SOS1 and to prevent reloading of RAS-family proteins with GTP, several different fragments were subsequently identified (Winter et al., J. Med. Chem. 2015, 58(5):2265-74). However, reversible binding of fragments to SOS1 did not translate into a measurable effect on the nucleotide exchange and only a weak effect was observed for fragments covalently bound to RAS.

[0011] Also recently, studies have been conducted to combine rational design and screening platforms to identify small molecule inhibitors of SOS1 (Evelyn et al., Chem. Biol. 2014, 21 (12):1618-28; Evelyn et al., J. Biol. Chem. 2015, 290(20):12879-98; Zheng et al., WO 2016/077793), i.e., compounds which bind to SOS1 and inhibit protein-protein interaction with RAS-family proteins. Although compounds with a slight inhibitory effect on SOS1 have been identified, the effects on guanine nucleotide exchange and cellular signal transduction modulation (e.g., ERK phosphorylation) are weak.

BRIEF SUMMARY

[0011a] In an aspect of the present disclosure, there is provided a compound having the structure of Formula (I),



(I)

or a pharmaceutically acceptable salt, solvate, ~~isomer, prodrug~~stereoisomer, or tautomer thereof, wherein:

Q^1 and Q^2 are independently CH or N;

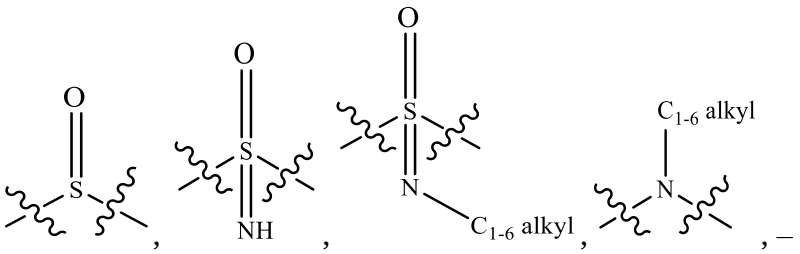
Q^3, Q^4, and Q^7 are independently C or N, wherein at least one of Q^3 and Q^4 is C and wherein Q^3, Q^4, and Q^7 are not all N;

Q^5 is CH, N, NH, O, or S;

Q^6 is CH, N, NH, N-C_{1-6} alkyl, N-C_{1-6} heteroalkyl, N-(3-7 membered cycloalkyl), N-(3-7 membered heterocyclyl), O, or S;

wherein at least one of Q^1, Q^2, Q^3, Q^4, Q^5, Q^6, and Q^7 is N, NH, O, or S;

R^1 is selected from the group consisting of H, C_{1-6} alkyl, halogen, -NHR^{1a}, –OR^{1a}, cyclopropyl, and –CN; wherein C_{1-6} alkyl is optionally substituted with halogen, -NHR^{1a}, or –OR^{1a}; wherein R^{1a} is H, C_{1-6} alkyl, 3-6 membered heterocyclyl, or C_{1-6} haloalkyl;

L^2 is selected from the group consisting of a bond, –C(O)–, –C(O)O–, –C(O)$NH(CH_2)_o$–, –$S(O)_2$–,  , –C(O)$(CH_2)_p$–, –$(CH_2)_p$–, and –O–; wherein o is 0, 1, or 2; and wherein p is a number from 1 to 6;

R^2 is selected from the group consisting of ~~H,~~ C_{1-6} alkyl, C_{2-6} alkenyl, -$NR^{2b}R^{2c}$, -OR^{2a}, 3-14 membered cycloalkyl, 3-14 membered cycloalkenyl, 3-14 membered heterocyclyl, ~~6-10 membered aryl,~~ and 5-10 membered heteroaryl; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, 3-14 membered cycloalkyl, 3-14 membered cycloalkenyl, 3-14 membered heterocyclyl, ~~6-10 membered aryl,~~ and 5-10 membered heteroaryl are independently optionally substituted with C_{1-6} alkyl, C_{1-6} haloalkyl, –OH, -OR^{2a}, oxo, halogen, –C(O)R^{2a}, –C(O)OR^{2a}, –C(O)$NR^{2b}R^{2c}$, –CN, -$NR^{2b}R^{2c}$, 3-6 membered cycloalkyl, 3-7 membered heterocyclyl, 6-10 membered aryl, or 5-10 membered heteroaryl;

wherein R^{2a} is H, C_{1-6} alkyl, C_{1-6} haloalkyl, 3-7 membered heterocyclyl, or –$(CH_2)_rOCH_3$, wherein r is 1, 2, or 3;

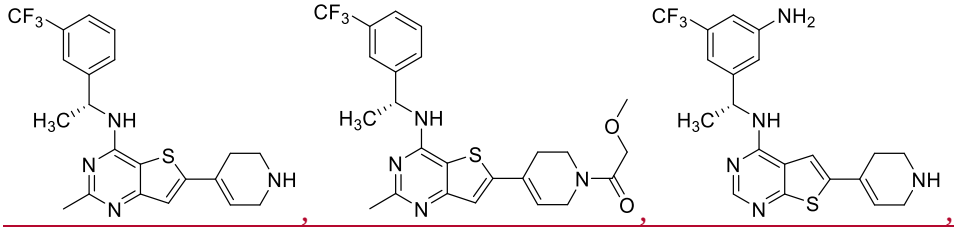
wherein R^{2b} is H or C_{1-6} alkyl;

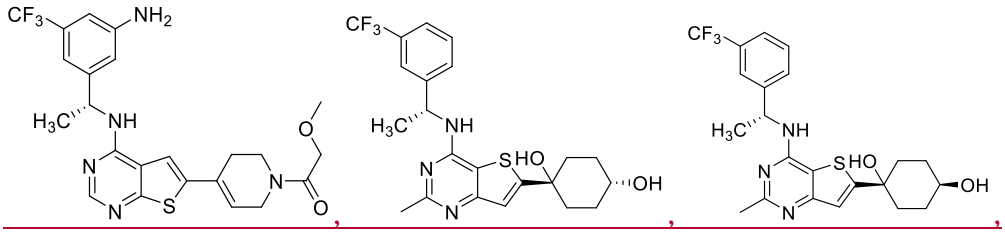
wherein R^{2c} is H or C_{1-6} alkyl;

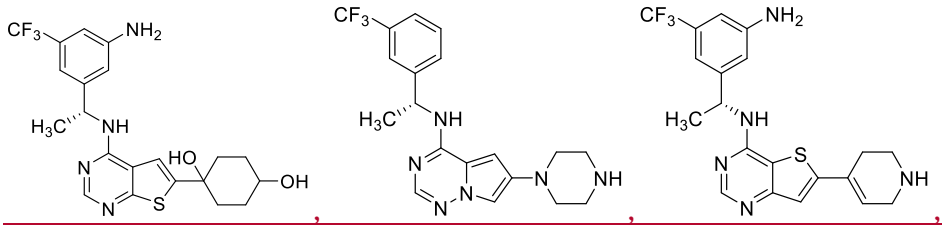
at least one of R^3 and R^4 is H and at least one of R^3 and R^4 is CH_3~~R^3 and R^4 are independently H or C_{1-6}alkyl optionally substituted with halo or -OH; wherein at least one of R^3 and R^4 is H or wherein R^3 and R^4 together with the atom to which they are attached combine to form a 3-6 membered cycloalkyl~~; and

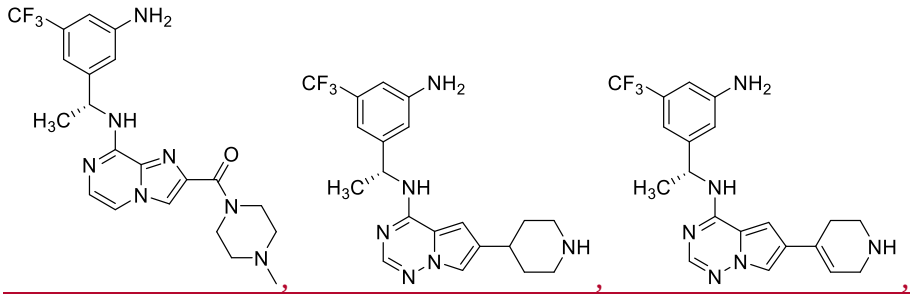
A is a~~n optionally~~ substituted 6-membered aryl~~ or an optionally substituted 5-6 membered heteroaryl~~.

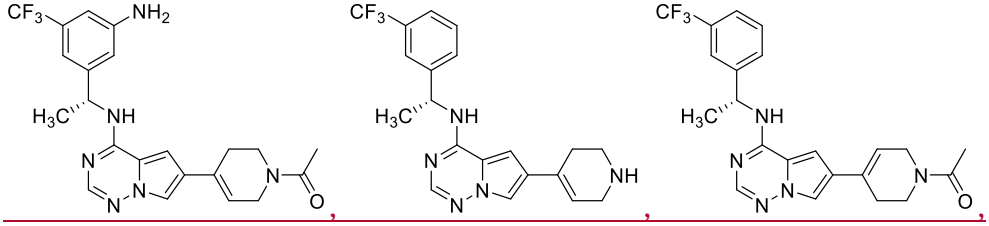
[0011b] In another aspect of the present disclosure, there is provided a compound, or a pharmaceutically acceptable salt, solvate, ~~hydrate~~stereoisomer, or tautomer~~, or isomer~~ thereof, selected from the group consisting of the following compounds~~ of Collection 1~~:

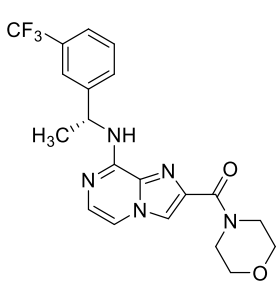
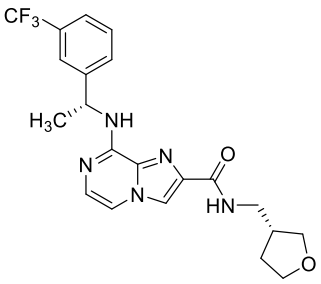
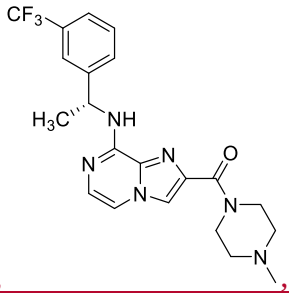


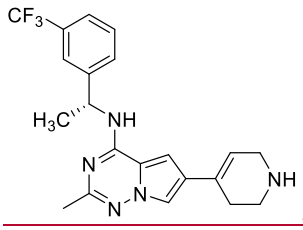
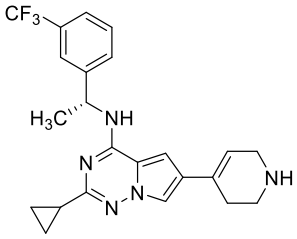
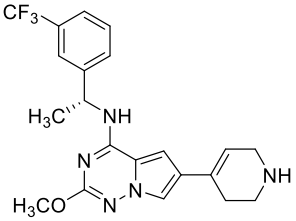


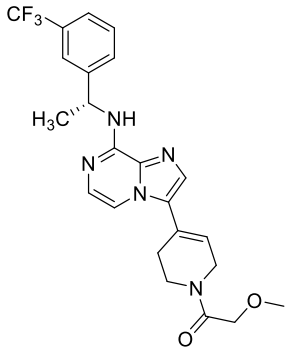
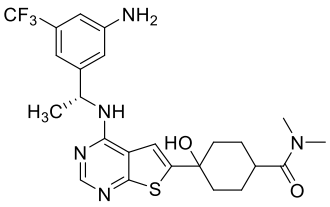
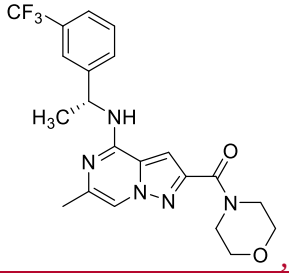


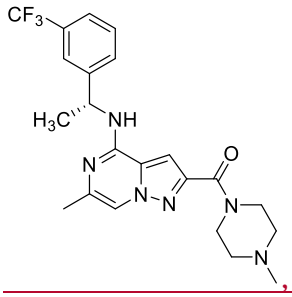
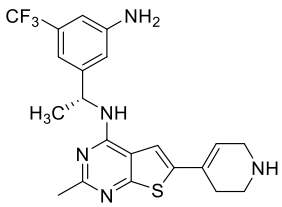
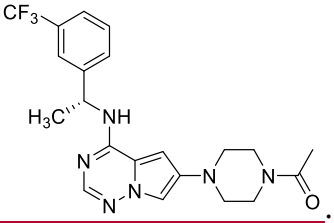




 ,  ,  ,

 ,  ,  ,

 ,  ,  ,

 ,  , and  .

[0011c] In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, ~~hydrate~~stereoisomer, or tautomer~~, or isomer~~ thereof, and a pharmaceutically acceptable carrier.

~~**[0011d]** In another aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or isomer thereof, in the manufacture of a medicament for inhibiting SOS1 in a subject.~~

~~**[0011e]** In a further aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or isomer thereof, in the manufacture of a medicament for inhibiting the interaction of SOS1 and a RAS-family protein in a cell or inhibiting the interaction of SOS1 and RAC1 in a cell.~~

~~**[0011f]** In another aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or isomer thereof, in the manufacture of a medicament for treating or preventing a disease, wherein treating or preventing the disease is characterized by inhibition of the interaction of SOS1 and a RAS-family protein or by inhibition of the interaction of SOS1 and RAC1.~~

[~~0011g~~0011d] In ~~a further~~another aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, ~~hydrate~~stereoisomer, or tautomer~~, or isomer~~ thereof, in the manufacture of a medicament for treating or preventing cancer in a subject in need thereof.

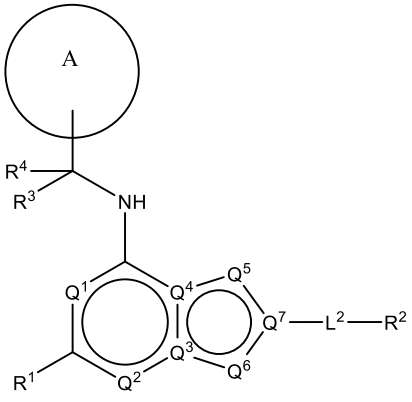
[~~0011h~~0011e] In ~~another~~ a further aspect of the present disclosure, there is provided a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, ~~hydrate~~stereoisomer, or tautomer~~, or isomer~~ thereof, for use in inhibiting SOS1 in a subject, or for use in inhibiting the interaction of SOS1 and a RAS-family protein in a cell or inhibiting the interaction of SOS1 and RAC1 in a cell, or for use in treating or preventing a disease, wherein treating or preventing the disease is characterized by inhibition of the interaction of SOS1 and a RAS-family protein or by inhibition of the interaction of SOS1 and RAC1, or for use in treating or preventing cancer in a subject in need thereof.

[0012] The present disclosure relates to compounds capable of inhibiting the activity of SOS1. The present disclosure further provides a process for the preparation of compounds, pharmaceutical preparations comprising such compounds and methods of using such compounds and compositions in the management of diseases or disorders associated with the aberrant activity of SOS1.

[0013] One example of the present disclosure relates to compounds of Formula (I):

We Claim:

1. A compound having the structure of Formula (I),



(I)

or a pharmaceutically acceptable salt, solvate, stereoisomer~~isomer, prodrug~~, or tautomer thereof, wherein:

Q^1 and Q^2 are independently CH or N;

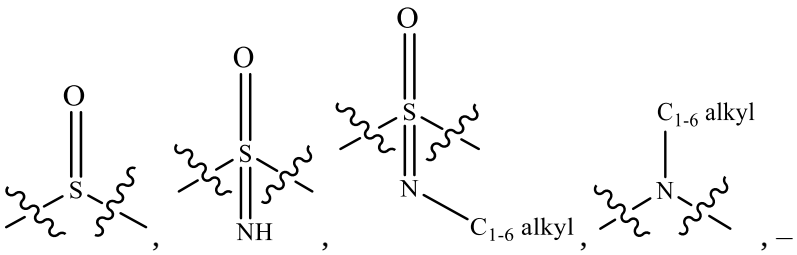
Q^3, Q^4, and Q^7 are independently C or N, wherein at least one of Q^3 and Q^4 is C and wherein Q^3, Q^4, and Q^7 are not all N;

Q^5 is CH, N, NH, O, or S;

Q^6 is CH, N, NH, N-C_{1-6} alkyl, N-C_{1-6} heteroalkyl, N-(3-7 membered cycloalkyl), N-(3-7 membered heterocyclyl), O, or S;

wherein at least one of Q^1, Q^2, Q^3, Q^4, Q^5, Q^6, and Q^7 is N, NH, O, or S;

R^1 is selected from the group consisting of H, C_{1-6} alkyl, halogen, -NHR^{1a}, –OR^{1a}, cyclopropyl, and –CN; wherein C_{1-6} alkyl is optionally substituted with halogen, -NHR^{1a}, or –OR^{1a}; wherein R^{1a} is H, C_{1-6} alkyl, 3-6 membered heterocyclyl, or C_{1-6} haloalkyl;

L^2 is selected from the group consisting of a bond, –C(O)–, –C(O)O–, –C(O)$NH(CH_2)_o$–, –$S(O)_2$–, 

, –

$C(O)(CH_2)_p$–, –$(CH_2)_p$–, and –O–; wherein o is 0, 1, or 2; and wherein p is a number from 1 to 6;

R^2 is selected from the group consisting of ~~H,~~ C_{1-6} alkyl, C_{2-6} alkenyl, -$NR^{2b}R^{2c}$, -OR^{2a}, 3-14 membered cycloalkyl, 3-14 membered cycloalkenyl, 3-14 membered heterocyclyl, ~~6-10 membered aryl,~~ and 5-10 membered heteroaryl; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, 3-14 membered cycloalkyl, 3-14 membered cycloalkenyl, 3-14 membered heterocyclyl, ~~6-10 membered aryl,~~ and 5-10 membered heteroaryl are independently optionally substituted with C_{1-6} alkyl, C_{1-6} haloalkyl, –OH, -OR^{2a}, oxo, halogen, –$C(O)R^{2a}$, –$C(O)OR^{2a}$, –$C(O)NR^{2b}R^{2c}$, –CN, -$NR^{2b}R^{2c}$, 3-6 membered cycloalkyl, 3-7 membered heterocyclyl, 6-10 membered aryl, or 5-10 membered heteroaryl;

wherein R^{2a} is H, C_{1-6} alkyl, C_{1-6} haloalkyl, 3-7 membered heterocyclyl, or –$(CH_2)_rOCH_3$, wherein r is 1, 2, or 3;

wherein R^{2b} is H or C_{1-6} alkyl;

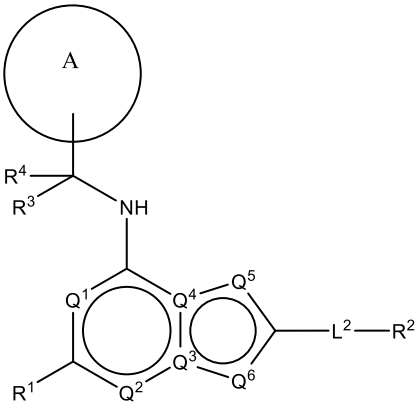
wherein R^{2c} is H or C_{1-6} alkyl;

~~R^3 and R^4 are independently H or C_{1-6} alkyl optionally substituted with halo or -OH; wherein~~ at least one of R^3 and R^4 is H and at least one of~~or wherein~~ R^3 and R^4 is CH_3~~together with the atom to which they are attached combine to form a 3-6 membered cycloalkyl~~; and

A is a ~~an optionally~~ substituted 6-membered aryl~~ or an optionally substituted 5-6 membered heteroaryl~~.

2. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, stereoisomer~~isomer, prodrug~~, or tautomer thereof, wherein no more than five of Q^1, Q^2, Q^3, Q^4, Q^5, Q^6, and Q^7 is N, NH, NCH_3, O, or S.

3. The compound of claim 1 having the structure of Formula (I-a),



(I-a)

or a pharmaceutically acceptable salt, solvate, stereoisomer~~isomer, prodrug~~, or tautomer thereof, wherein:

Q^1, Q^2, Q^5 and A are as defined in claim 1;

Q^3 and Q^4 are independently C or N, wherein at least one of Q^3 and Q^4 is C;

Q^6 is CH, N, NH, O, or S;

wherein at least one of Q^1, Q^2, Q^3, Q^4, Q^5, and Q^6 is N, NH, O, or S;

R^1 is selected from the group consisting of H, halogen, C_{1-6} alkyl, cyclopropyl, –CN, and $–OR^{1a}$; wherein R^{1a} is H or C_{1-6} alkyl;

L^2 is selected from the group consisting of a bond, –C(O)–, –C(O)O–, $–C(O)NH(CH_2)_o–$, $–S(O)_2–$, $–C(O)(CH_2)_p–$, $–(CH_2)_p–$, and –O–; wherein o is 0, 1, or 2; and wherein p is a number from 1 to 6;

R^2 is selected from the group consisting of ~~H, –~~$(CH_2)_qCH_3$, 3-14 membered cycloalkyl, 3-14 membered cycloalkenyl, 3-14 membered heterocyclyl, ~~6-10 membered aryl,~~ and 5-10 membered heteroaryl; wherein q is a number from 1 to 5; wherein each 3-14 membered cycloalkyl, 3-14 membered cycloalkenyl, 3-14 membered heterocyclyl, ~~6-10 membered aryl,~~ or 5-10 membered heteroaryl is optionally substituted with C_{1-6} alkyl, –OH, halogen, $–C(O)R^{2a}$, or $–C(O)NR^{2b}R^{2c}$; wherein R^{2a} is C_{1-6} alkyl or $–(CH_2)_rOCH_3$, wherein r is 1, 2, or 3; wherein R^{2b} is H or C_{1-6} alkyl; and wherein R^{2c} is H or C_{1-6} alkyl; and

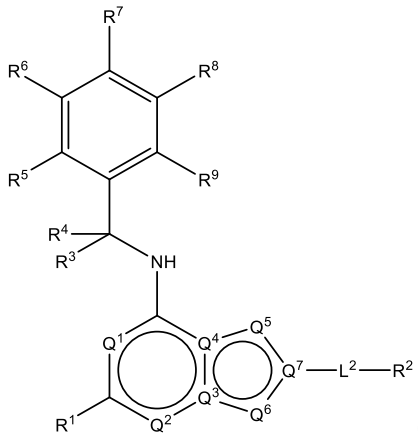
at least one of R^3 and R^4 is H and at least one of R^3 and R^4 is CH_3~~R^3 and R^4 are independently H or C_{1-6} alkyl; wherein at least one of R^3 and R^4 is not H; or R^3 and R^4~~

~~together with the atom to which they are attached combine to form a 3-6 membered cycloalkyl~~.

~~4. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt, solvate, isomer, prodrug, or tautomer thereof, wherein A is an optionally substituted 6-membered aryl.~~

~~5. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt, solvate, isomer, prodrug, or tautomer thereof, wherein A is an optionally substituted 5-6 membered heteroaryl.~~

~~6~~4. The compound of claim 1 having the structure of Formula (II),



(II)

or a pharmaceutically acceptable salt, solvate, stereoisomer~~isomer, prodrug~~, or tautomer thereof, wherein:

L^2, Q^1, Q^2, Q^3, Q^4, Q^5, Q^6, Q^7, R^1, R^2, R^3 and R^4 are as defined in claim 1;

R^5, R^6, R^7, R^8, and R^9 are independently selected from the group consisting of H, D, C_{1-6} alkyl, C_{2-6} alkenyl, 4-8 membered cycloalkenyl, C_{2-6} alkynyl, 3-8 membered cycloalkyl, -OH, halogen, $–NO_2$, –CN, $–NR^{11}R^{12}$, $–SR^{10}$, $–S(O)_2NR^{11}R^{12}$, $–S(O)_2R^{10}$, $–NR^{10}S(O)_2NR^{11}R^{12}$, $–NR^{10}S(O)_2R^{11}$, $–S(O)NR^{11}R^{12}$, $–S(O)R^{10}$, $–NR^{10}S(O)NR^{11}R^{12}$, $–NR^{10}S(O)R^{11}$, $–C(O)R^{10}$, and $–CO_2R^{10}$, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, 4-8 membered cycloalkenyl, C_{2-6} alkynyl, and 3-8 membered cycloalkyl are independently optionally substituted with –OH, halogen, $–NO_2$, oxo, –CN, $–R^{10}$, $–OR^{10}$, $–NR^{11}R^{12}$, $–SR^{10}$, $–S(O)_2NR^{11}R^{12}$, $–S(O)_2R^{10}$, $–NR^{10}S(O)_2NR^{11}R^{12}$, $–NR^{10}S(O)_2R^{11}$, $–S(O)NR^{11}R^{12}$, –

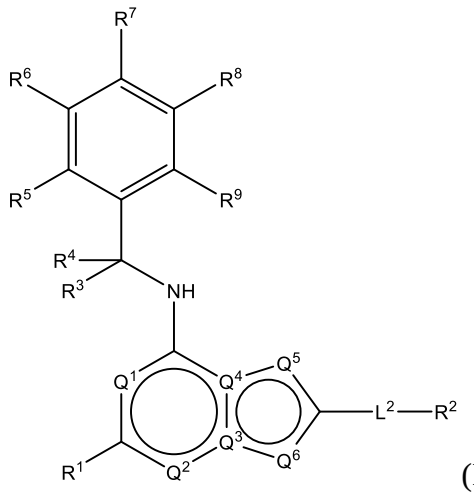
$S(O)R^{10}$, $–NR^{10}S(O)NR^{11}R^{12}$, $–NR^{10}S(O)R^{11}$, 3-14 membered heterocyclyl, 6-10 membered aryl, or 5-10 membered heteroaryl;

R^{10}, R^{11}, and R^{12} are at each occurrence independently selected from H, D, C_{1-6} alkyl, C_{2-6} alkenyl, 4-8 membered cycloalkenyl, C_{2-6} alkynyl, 3-8 membered cycloalkyl, 3-14 membered heterocyclyl, $–OR^{13}$, $–SR^{13}$, halogen, $–NR^{13}R^{14}$, $–NO_2$, and –CN; and

R^{13} and R^{14} are at each occurrence independently selected from H, D, C_{1-6} alkyl, C_{2-6} alkenyl, 4-8 membered cycloalkenyl, C_{2-6} alkynyl, 3-8 membered cycloalkyl, and 3-14 membered heterocyclyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, 4-8 membered cycloalkenyl, C_{2-6} alkynyl, 3-8 membered cycloalkyl, and 3-14 membered heterocyclyl are independently optionally substituted with –OH, –SH, $–NH_2$, $–NO_2$, or –CN.

~~7~~5. The compound of claim ~~6~~4, or a pharmaceutically acceptable salt, solvate, stereoisomer~~isomer, prodrug~~, or tautomer thereof, wherein no more than five of Q^1, Q^2, Q^3, Q^4, Q^5, Q^6, and Q^7 is N, NH, NCH_3, O, or S.

~~8~~6. The compound of claim ~~6~~ 4 having the structure of Formula (II-a),



(II-a)

or a pharmaceutically acceptable salt, solvate, stereoisomer~~isomer, prodrug~~, or tautomer thereof, wherein:

Q^1, Q^2, Q^5, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13} and R^{14} are as defined in claim ~~6~~4;

Q^3 and Q^4 are independently C or N, wherein at least one of Q^3 and Q^4 is C;

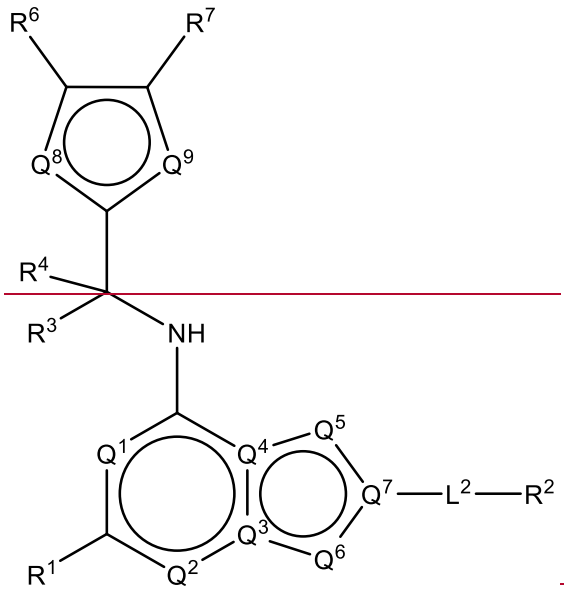
Q^6 is CH, N, NH, O, or S;

wherein at least one of Q^1, Q^2, Q^3, Q^4, Q^5, and Q^6 is N, NH, O, or S;

R^1 is selected from the group consisting of H, halogen, C_{1-6} alkyl, cyclopropyl, –CN, and $–OR^{1a}$; wherein R^{1a} is H or C_{1-6} alkyl; and

L^2 is selected from the group consisting of a bond, –C(O)–, –C(O)O–, $–C(O)NH(CH_2)_o–$, $–S(O)_2–$, $–C(O)(CH_2)_p–$, $–(CH_2)_p–$, and –O–; wherein o is 0, 1, or 2; and wherein p is a number from 1 to 6.

~~9. The compound of claim 1 having the structure of Formula (III),~~



~~(III)~~

~~or a pharmaceutically acceptable salt, solvate, isomer, prodrug, or tautomer thereof, wherein:~~

~~L^2, Q^1, Q^2, Q^3, Q^4, Q^5, Q^6, Q^7, R^1, R^2, R^3 and R^4 are as defined in claim 1;~~

~~Q^8 and Q^9 are independently CH, N, NH, O, or S, provided at least one of Q^8 and Q^9 is N, NH, O, or S;~~

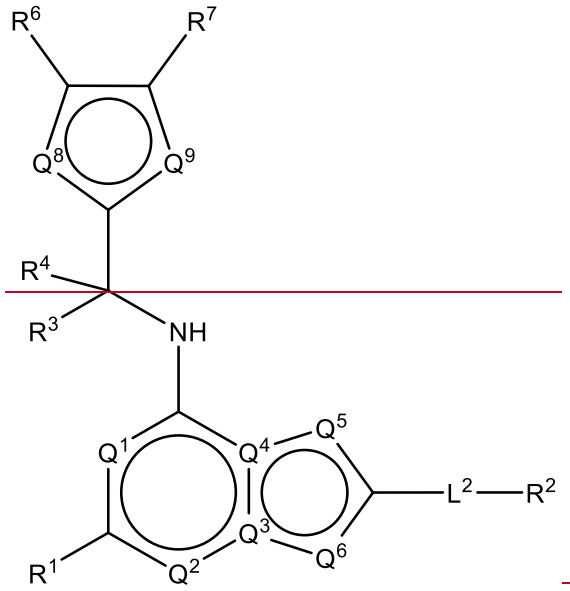
~~R^6 and R^7 are independently selected from the group consisting of H, D, C_{1-6} alkyl, C_{2-6} alkenyl, 4-8 membered cycloalkenyl, C_{2-6} alkynyl, 3-8 membered cycloalkyl, OH, halogen, NO_2, CN, $NR^{11}R^{12}$, SR^{10}, $S(O)_2NR^{11}R^{12}$, $S(O)_2R^{10}$, $NR^{10}S(O)_2NR^{11}R^{12}$, $NR^{10}S(O)_2R^{11}$, $S(O)NR^{11}R^{12}$, $S(O)R^{10}$, $NR^{10}S(O)NR^{11}R^{12}$, $NR^{10}S(O)R^{11}$, $C(O)R^{10}$,~~

and $-CO_2R^{10}$, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, 4-8 membered cycloalkenyl, C_{2-6} alkynyl, and 3-8 membered cycloalkyl are independently optionally substituted with -OH, halogen, $-NO_2$, oxo, -CN, $=R^{10}$, $-OR^{10}$, $-NR^{11}R^{12}$, $=SR^{10}$, $-S(O)_2NR^{11}R^{12}$, $-S(O)_2R^{10}$, $-NR^{10}S(O)_2NR^{11}R^{12}$, $-NR^{10}S(O)_2R^{11}$, $-S(O)NR^{11}R^{12}$, $-S(O)R^{10}$, $-NR^{10}S(O)NR^{11}R^{12}$, $-NR^{10}S(O)R^{11}$, 3-14 membered heterocyclyl, 6-10 membered aryl, or 5-10 membered heteroaryl;

R^{10}, R^{11}, and R^{12} are at each occurrence independently selected from H, D, C_{1-6} alkyl, C_{2-6} alkenyl, 4-8 membered cycloalkenyl, C_{2-6} alkynyl, 3-8 membered cycloalkyl, 3-14 membered heterocyclyl, $-OR^{13}$, $-SR^{13}$, halogen, $-NR^{13}R^{14}$, $-NO_2$, or -CN; and

R^{13} and R^{14} are at each occurrence independently selected from H, D, C_{1-6} alkyl, C_{2-6} alkenyl, 4-8 membered cycloalkenyl, C_{2-6} alkynyl, 3-8 membered cycloalkyl, or 3-14 membered heterocyclyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, 4-8 membered cycloalkenyl, C_{2-6} alkynyl, 3-8 membered cycloalkyl, and 3-14 membered heterocyclyl are independently optionally substituted with -OH, -SH, $-NH_2$, $-NO_2$, or -CN.

10. The compound of claim 9 or a pharmaceutically acceptable salt, solvate, isomer, prodrug, or tautomer thereof, having the structure of Formula (III-a),

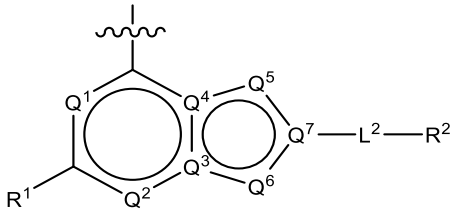


(III-a)

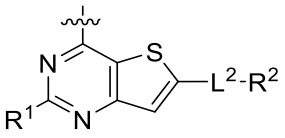
wherein L^2, Q^1, Q^2, Q^3, Q^4, Q^5, Q^6, Q^8, Q^9, R^1, R^2, R^3, R^4, R^6, and R^7 are as defined in claim 9.

~~11. The compound of claim 9, or a pharmaceutically acceptable salt, solvate, isomer, prodrug, or tautomer thereof, wherein no more than five of Q^1, Q^2, Q^3, Q^4, Q^5, Q^6, and Q^7 is N, NH, NCH_3, O, or S.~~

~~12~~7. The compound of any one of claims 1-~~11~~6, or a pharmaceutically acceptable salt, solvate, stereoisomer~~isomer, prodrug~~, or tautomer thereof, wherein:



is selected from the group consisting of:



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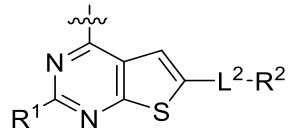

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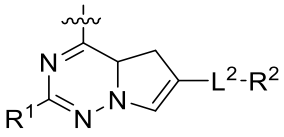

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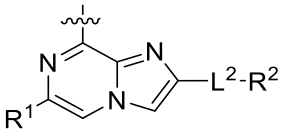

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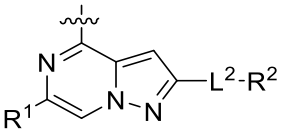

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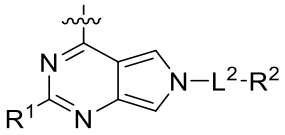

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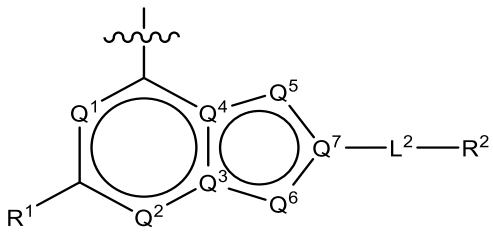
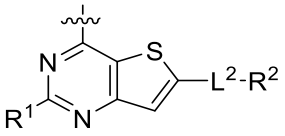
~~13~~8. The compound of any one of claims 1-~~11~~6, or a pharmaceutically acceptable salt, solvate, ~~isomer, prodrug~~stereoisomer, or tautomer thereof, wherein:



is selected from the group consisting of:

~~of:~~



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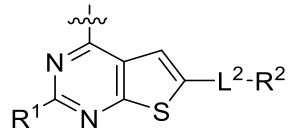

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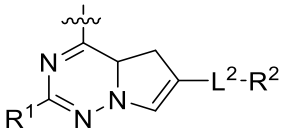

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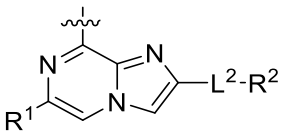

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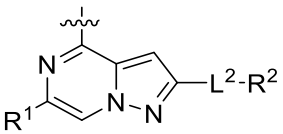

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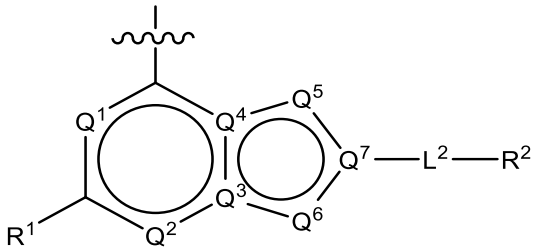
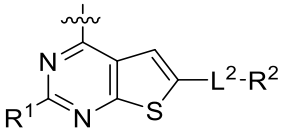
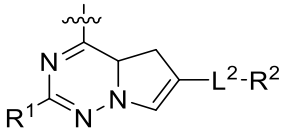
~~14~~9. The compound of any one of claims 1-~~11~~6, or a pharmaceutically acceptable salt, solvate, ~~isomer, prodrug~~stereoisomer, or tautomer thereof, wherein:



is selected from the group consisting of:



and



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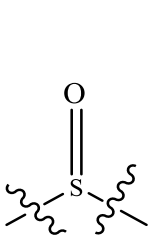
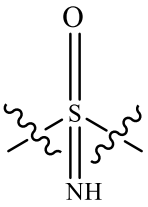
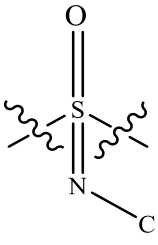
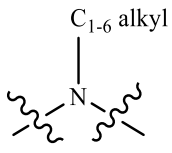
~~15~~10. The compound of any one of claims 1-~~14~~9, or a pharmaceutically acceptable salt, solvate, stereoisomer, ~~isomer, prodrug,~~ or tautomer thereof, wherein R^1 is H, halogen, $C_{1\text{-}6}$ alkyl, cyclopropyl, –CN, or $–OR^{1a}$; wherein R^{1a} is H or $C_{1\text{-}6}$ alkyl.

~~16~~11. The compound of any one of claims 1-~~15~~10, or a pharmaceutically acceptable salt, solvate, stereoisomer, ~~isomer, prodrug,~~ or tautomer thereof, wherein L^2 is selected from the group consisting of a bond, –C(O)–, –C(O)O–, $–C(O)NH(CH_2)_o–$, $–S(O)_2–$, $–C(O)(CH_2)_p–$, $–(CH_2)_p–$, and –O–; wherein o is 0, 1, or 2; and wherein p is a number from 1 to 6.

~~17~~12. The compound of any one of claims 1-~~15~~10, or a pharmaceutically acceptable salt, solvate, stereoisomer, ~~isomer, prodrug,~~ or tautomer thereof, wherein L^2 is selected from the group consisting of 

, 

, 

, and 

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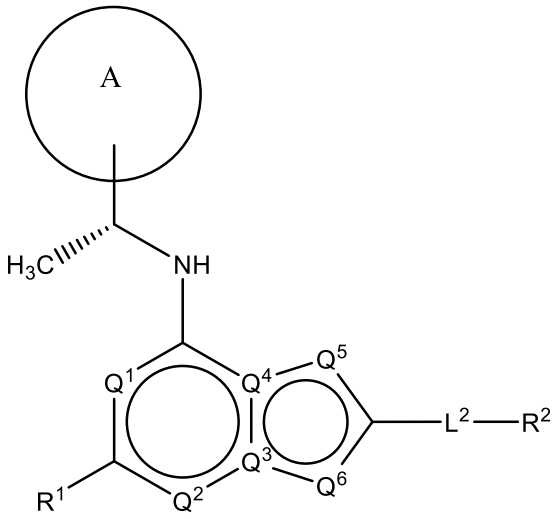
~~18~~13. The compound of any one of claims 1-~~17~~12, or a pharmaceutically acceptable salt, solvate, stereoisomer, ~~isomer, prodrug,~~ or tautomer thereof, wherein R^2 is

selected from the group consisting of H, C_{1-6} alkyl, -$NR^{2b}R^{2c}$, -OR^{2a}, 3-14 membered cycloalkyl, 3-14 membered cycloalkenyl, 3-14 membered heterocyclyl, ~~6-10 membered aryl,~~ and 5-10 membered heteroaryl; wherein each C_{1-6} alkyl, 3-14 membered cycloalkyl, 3-14 membered cycloalkenyl, 3-14 membered heterocyclyl, ~~6-10 membered aryl,~~ and 5-10 membered heteroaryl are independently optionally substituted with C_{1-6} alkyl,–OH, -OR^{2a}, oxo, halogen, –$C(O)R^{2a}$, –$C(O)OR^{2a}$, –$C(O)NR^{2b}R^{2c}$, –CN, -$NR^{2b}R^{2c}$, 3-6 membered cycloalkyl, 3-7 membered heterocyclyl, 6-10 membered aryl, or 5-10 membered heteroaryl.

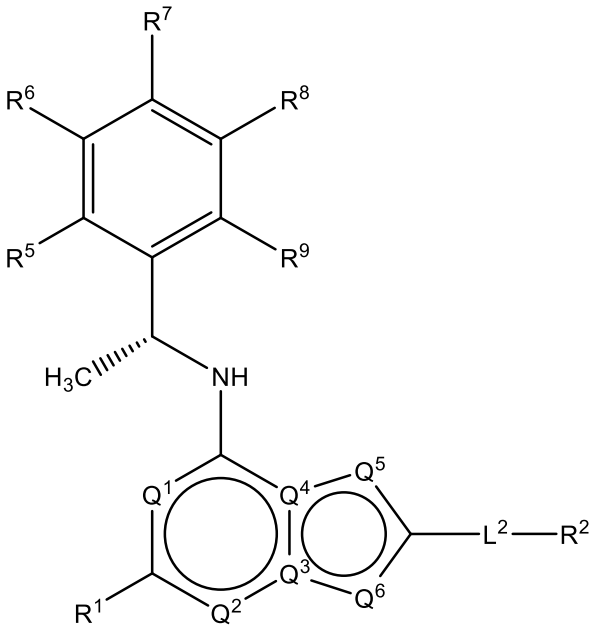
~~19~~14. The compound of any one of claims 1-~~17~~12, or a pharmaceutically acceptable salt, solvate, stereoisomer, ~~isomer, prodrug,~~ or tautomer thereof, wherein R^2 is selected from the group consisting of H, –$(CH_2)_qCH_3$, 3-14 membered cycloalkyl, 3-14 membered cycloalkenyl, 3-14 membered heterocyclyl, ~~6-10 membered aryl,~~ and 5-10 membered heteroaryl; wherein q is a number from 1 to 5; wherein each 3-14 membered cycloalkyl, 3-14 membered cycloalkenyl, 3-14 membered heterocyclyl, ~~6-10 membered aryl,~~ and 5-10 membered heteroaryl is independently optionally substituted with C_{1-6} alkyl, –OH, halogen, –$C(O)R^{2a}$, or –$C(O)NR^{2b}R^{2c}$; wherein R^{2a} is C_{1-6} alkyl or –$(CH_2)_rOCH_3$, wherein r is 1, 2, or 3; wherein R^{2b} is H or C_{1-6} alkyl; and wherein R^{2c} is H or C_{1-6} alkyl.

~~20~~15. The compound of claim 3, or a pharmaceutically acceptable salt, solvate, stereoisomer, ~~isomer, prodrug,~~ or tautomer thereof, wherein R^3 is H and R^4 is –CH_3 and the compound is of the following formula:



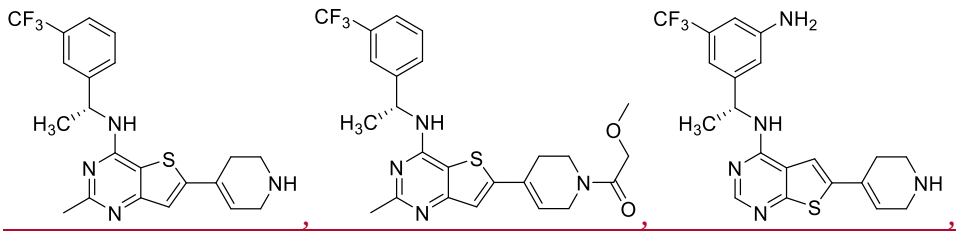
wherein A, L^2, Q^1, Q^2, Q^3, Q^4, Q^5, Q^6, R^1, R^2, m and n are as defined in claim 3.

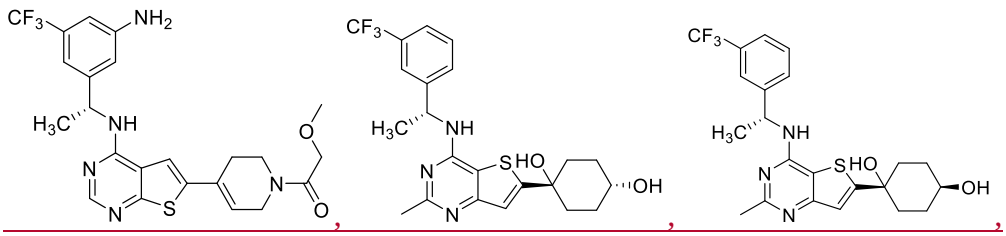
~~21~~16. The compound of claim ~~6~~8, or a pharmaceutically acceptable salt, solvate, stereoisomer, ~~isomer, prodrug,~~ or tautomer thereof, wherein R^3 is H and R^4 is $–CH_3$ and the compound is of the following formula:

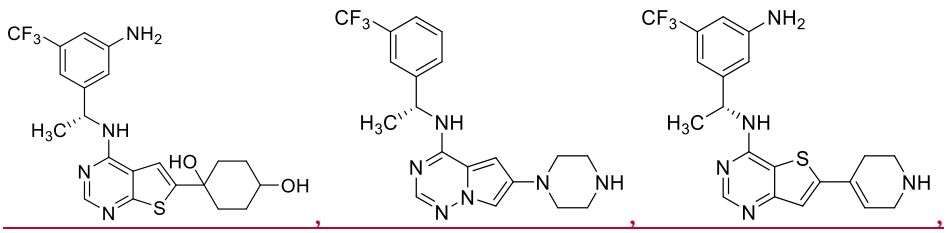


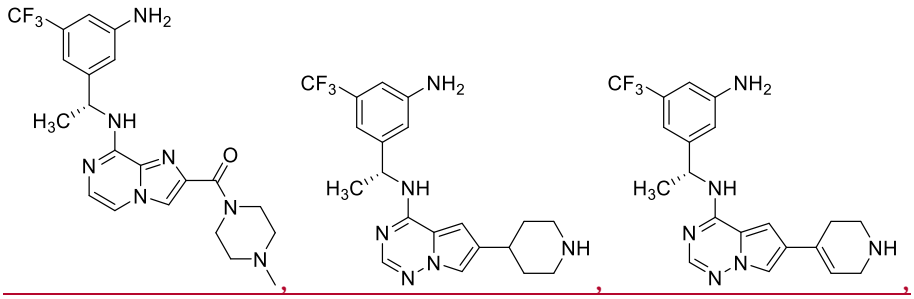
wherein L^2, Q^1, Q^2, Q^3, Q^4, Q^5, Q^6, R^1, R^2, R^4, R^5, R^6, R^7, R^8, R^9, m and n are as defined in claim ~~8~~6.

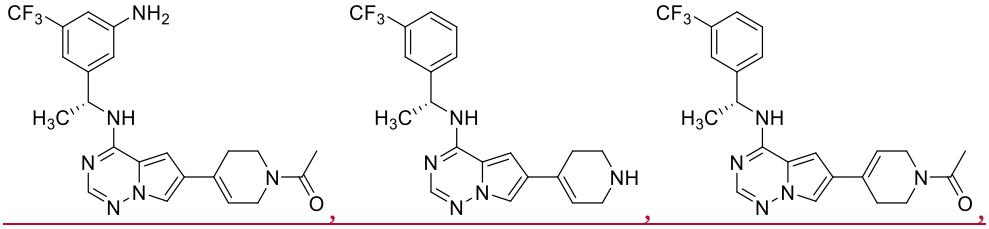
~~22~~17. A compound, or a pharmaceutically acceptable salt, solvate, ~~hydrate,~~ stereoisomer, or tautomer~~, or isomer~~ thereof, selected from the group consisting of the following compounds~~ of Collection 1~~:

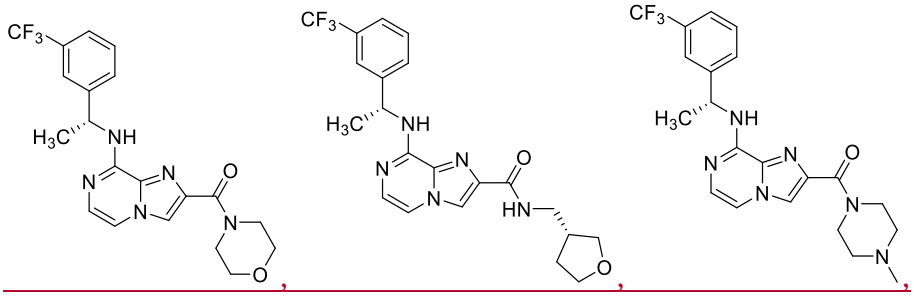


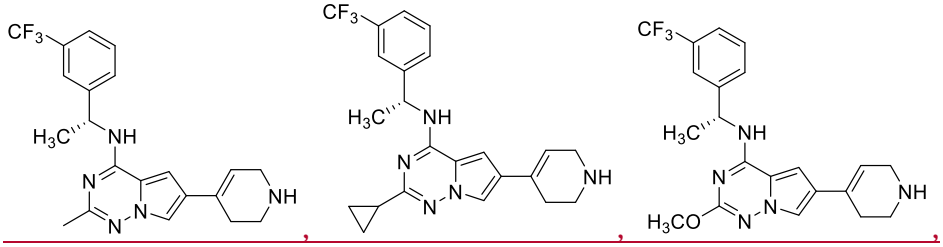


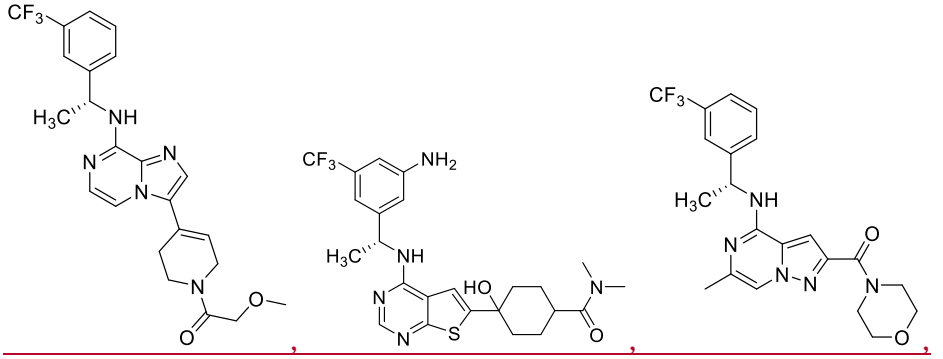


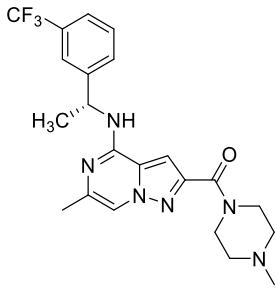


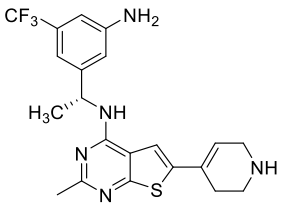


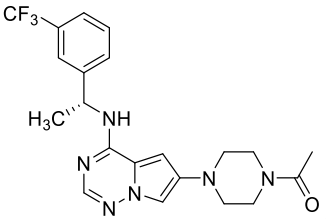








, 

, and 

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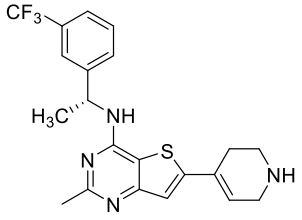
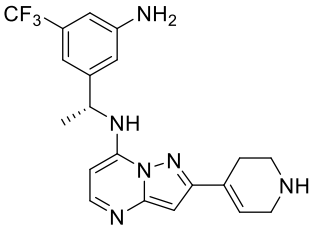
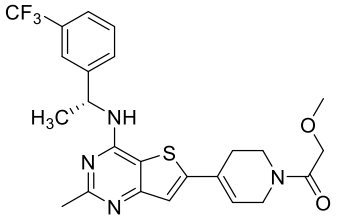
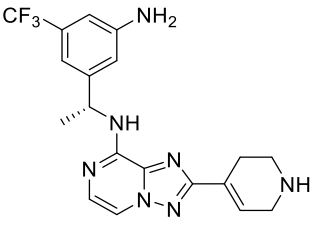
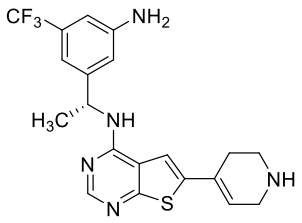
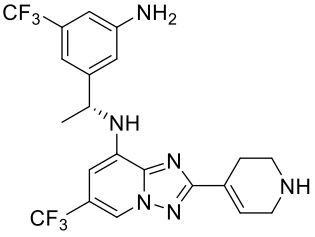
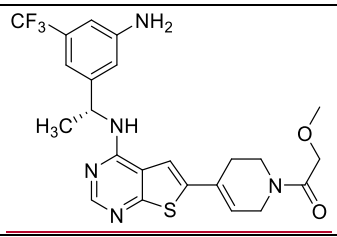
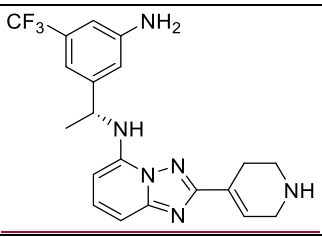
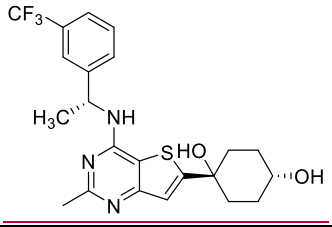
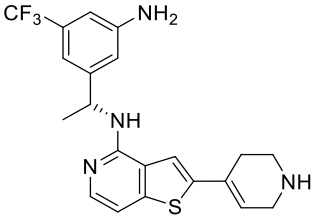
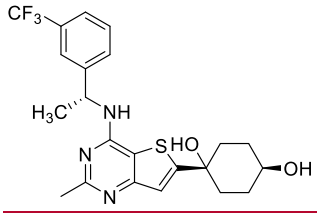
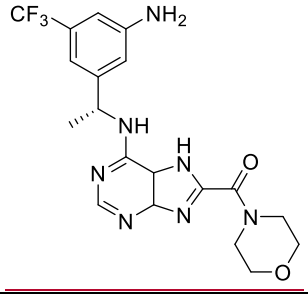
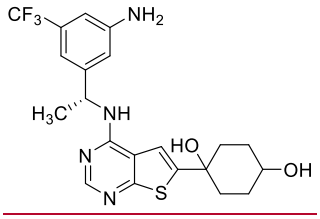
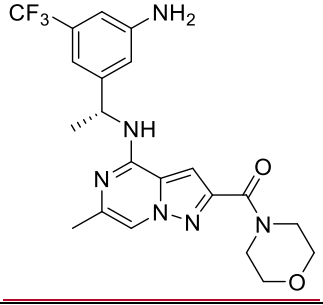
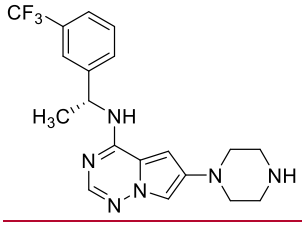
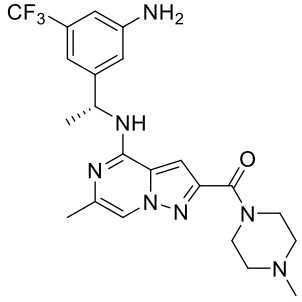
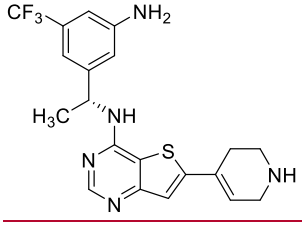
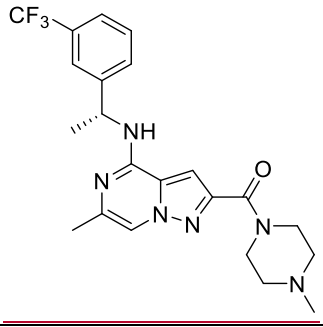
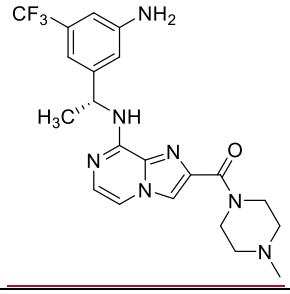
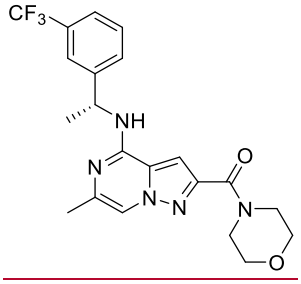
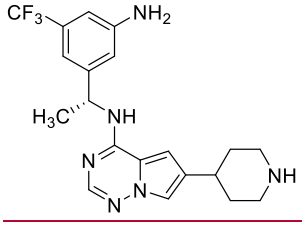
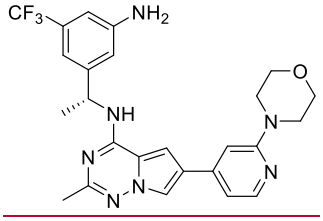
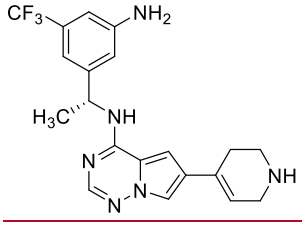
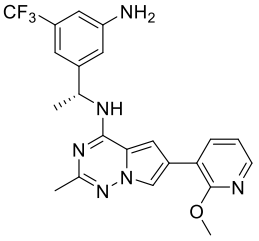
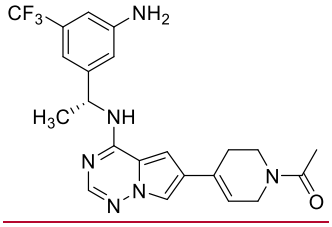
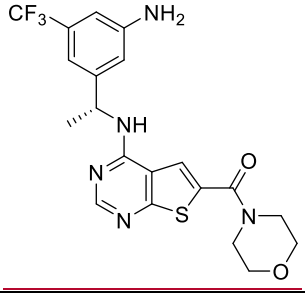
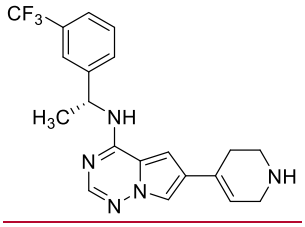
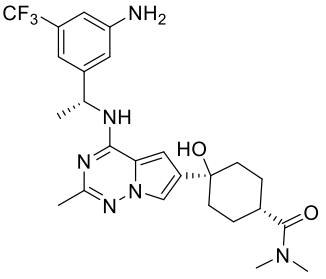
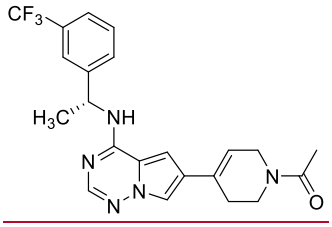
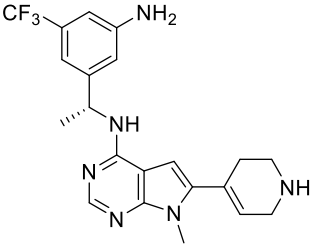
~~23. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or isomer thereof, selected from the group consisting of compounds of Collection 3.~~

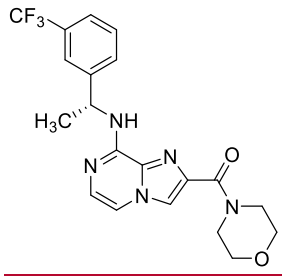
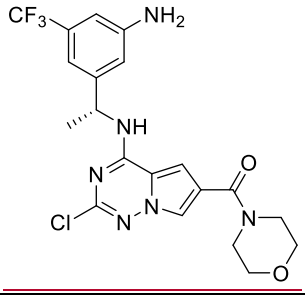
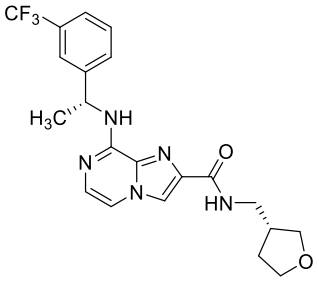
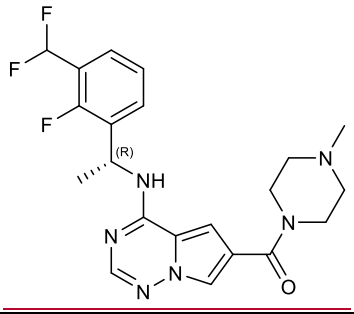
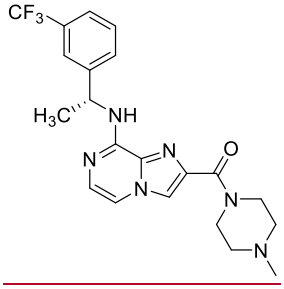
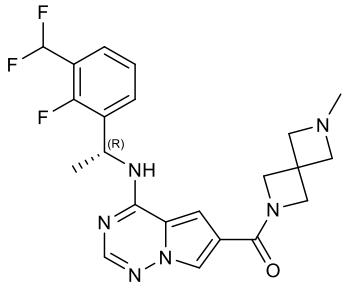
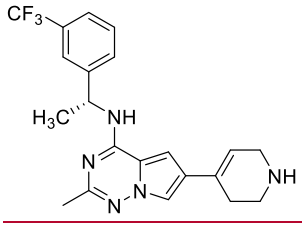
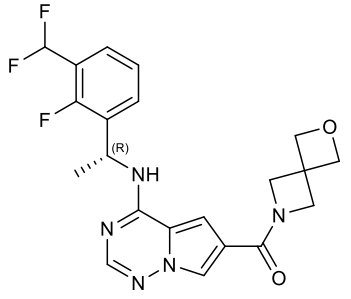
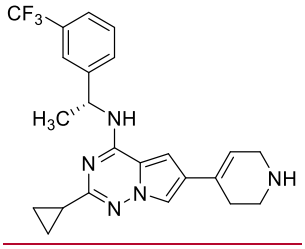
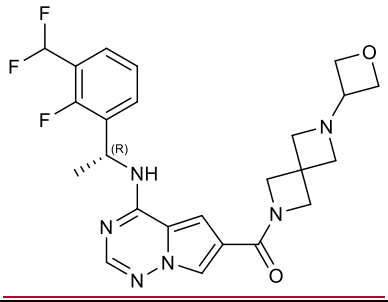
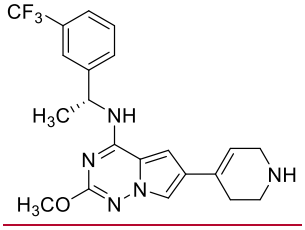
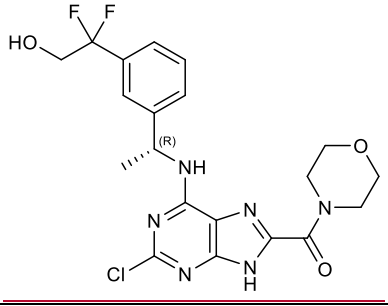
~~24. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or isomer thereof, selected from the group consisting of compounds of Collection 4.~~

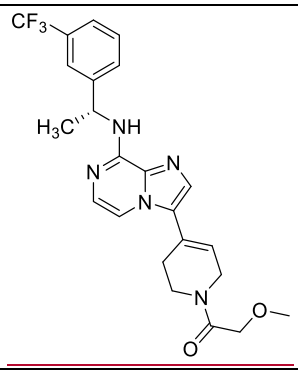
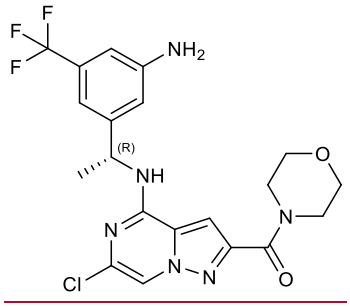
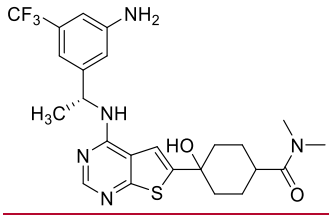
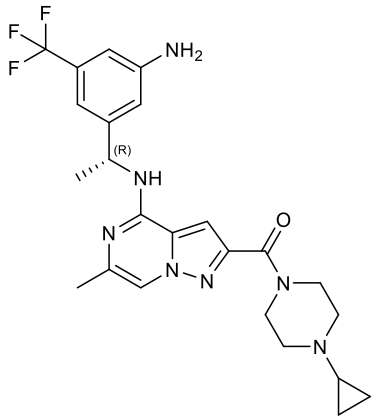
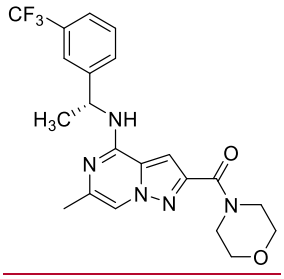
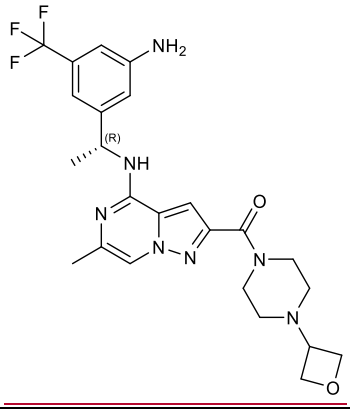
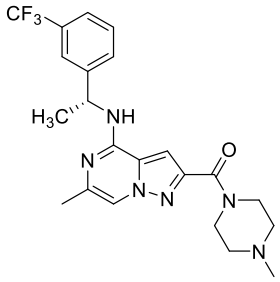
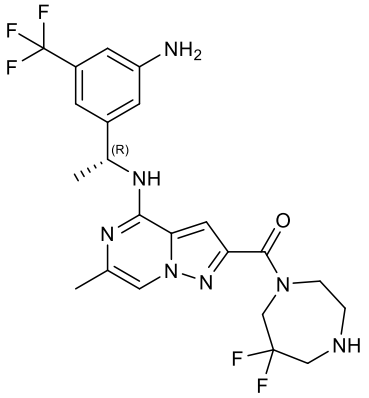
~~25~~18. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, ~~hydrate~~stereoisomer, or tautomer, ~~or isomer~~ thereof, selected from the group consisting of compounds ~~of~~ shown in the following Table: ~~A~~

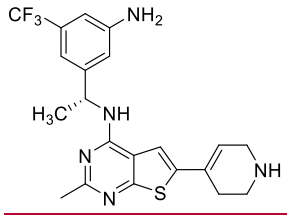
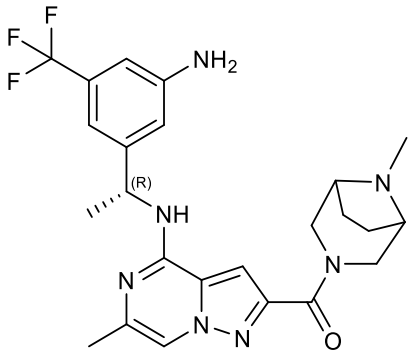
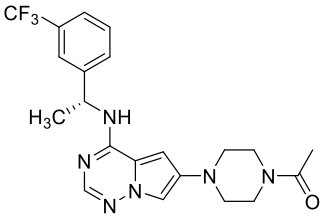
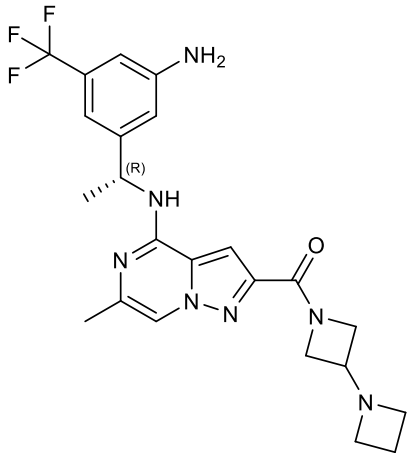
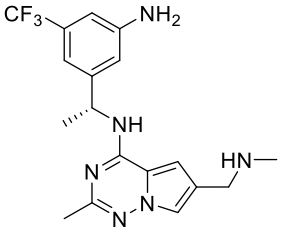
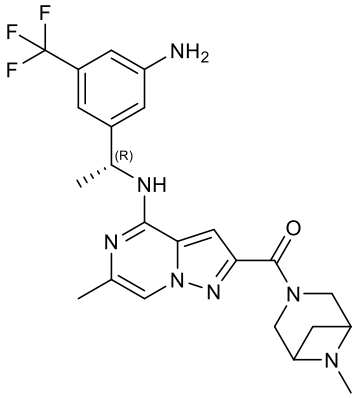
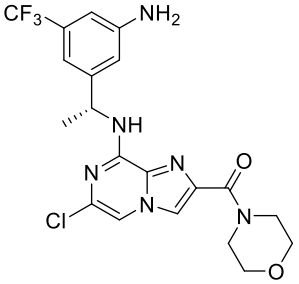
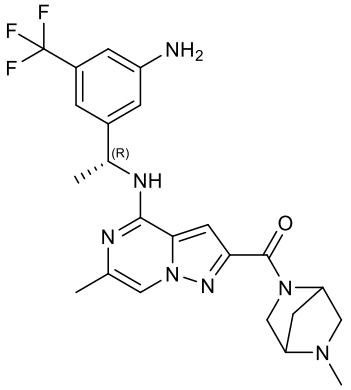
Example #	Structure	Example #	Structure
Example 1.		Example 52.	
Example 2.		Example 53.	
Example 3.		Example 54.	

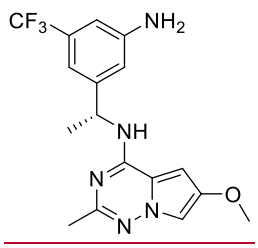
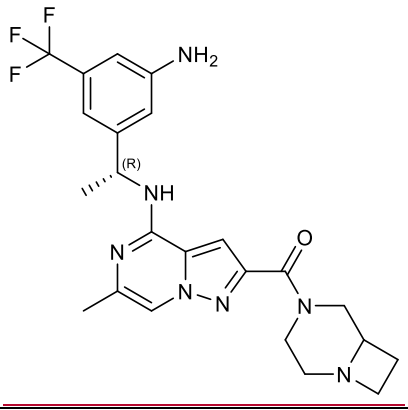
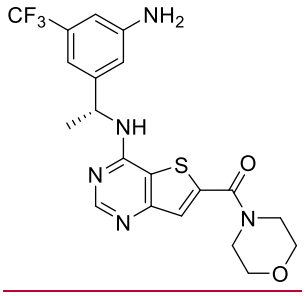
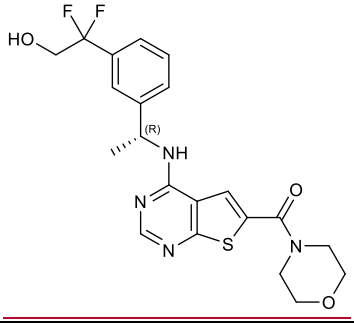
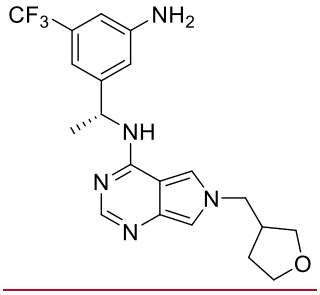
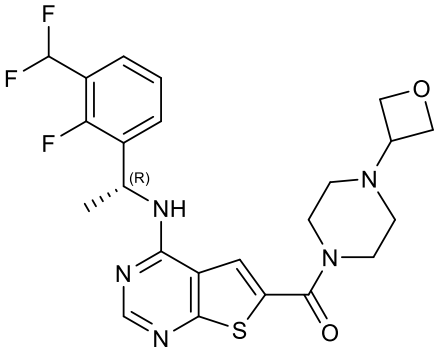
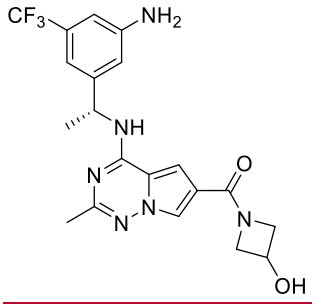
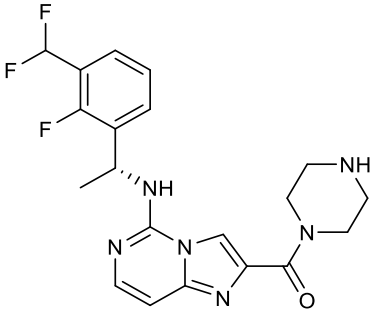
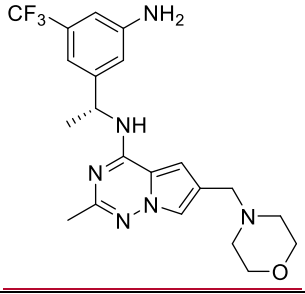
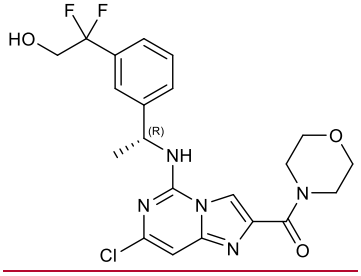
Example 4.		Example 55.	
Example 5.		Example 56.	
Example 6.		Example 57.	
Example 7.		Example 58., 60.	
Example 8.		Example 59.	
Example 9.		Example 61.	

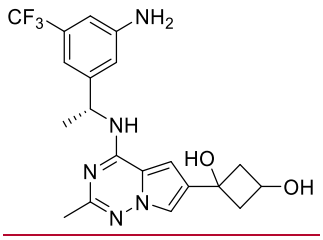
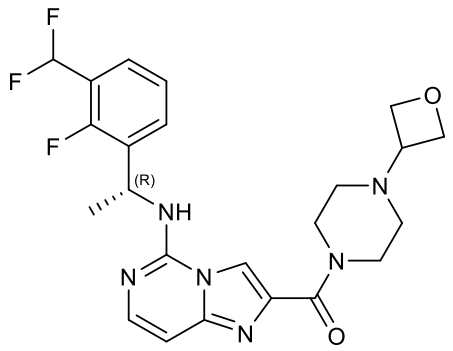
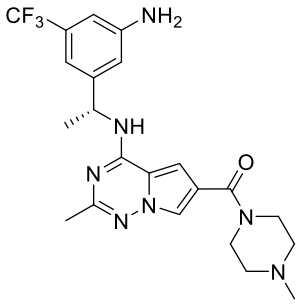
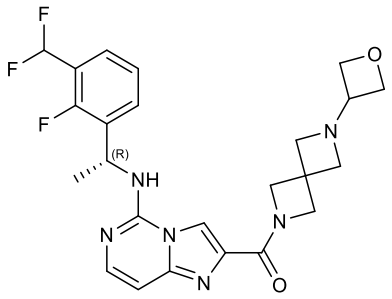
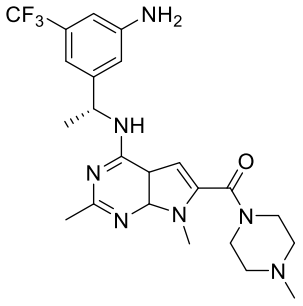
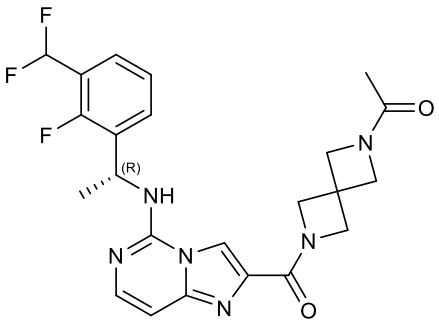
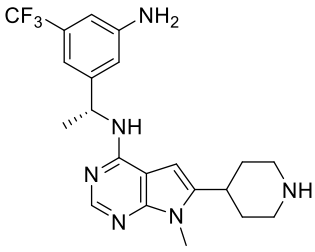
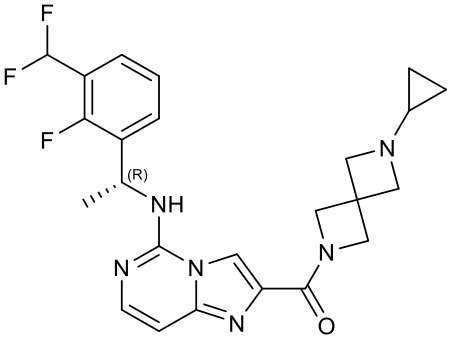
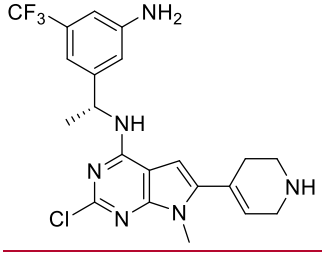
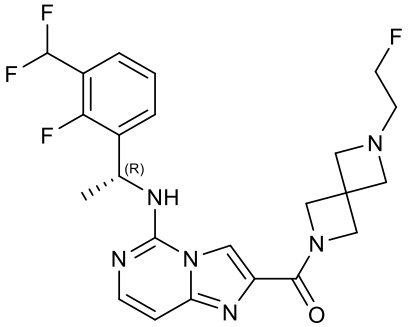
Example 10.		Example 62.	
Example 11.		Example 63.	
Example 12.		Example 64.	
Example 13.		Example 65.	
Example 14.		Example 66.	
Example 15.		Example 67.	

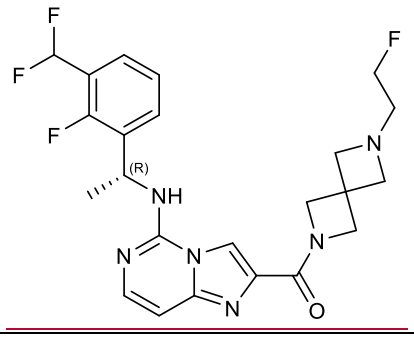
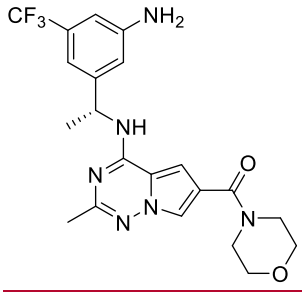
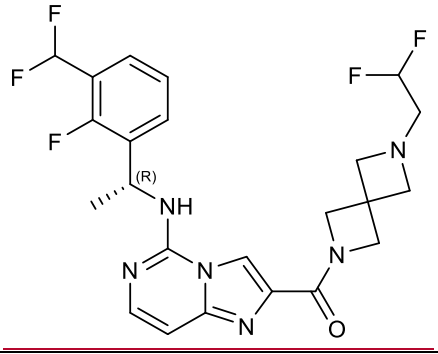
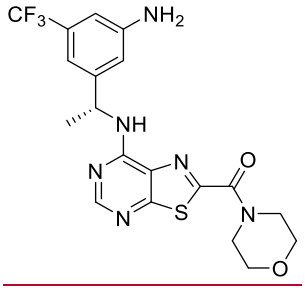
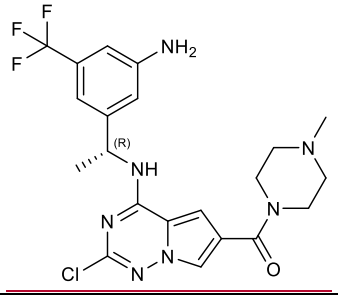
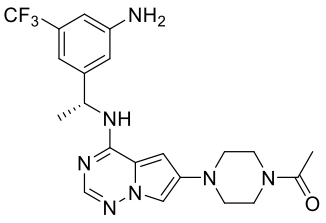
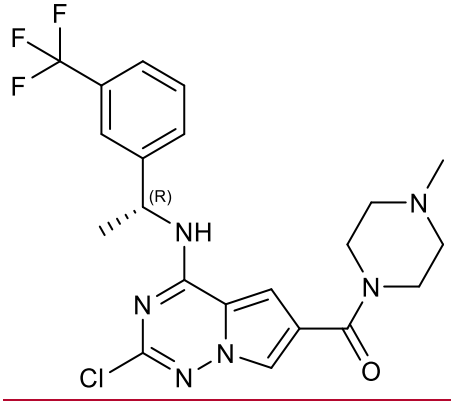
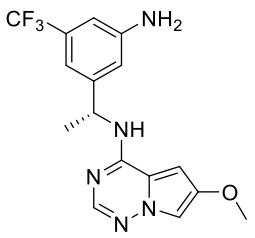
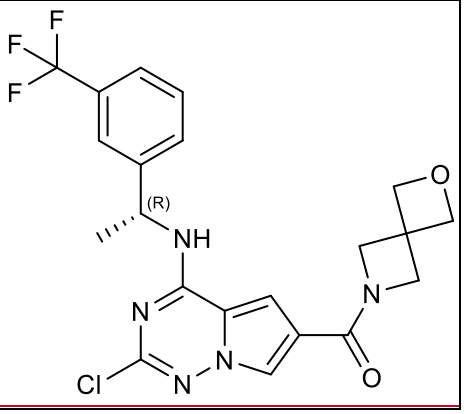
Example 16.		Example 68.	
Example 17.		Example 69.	
Example 18.		Example 70.	
Example 19.		Example 71.	
Example 20.		Example 72.	
Example 21.		Example 73.	

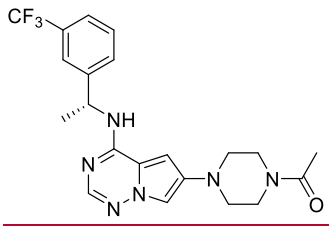
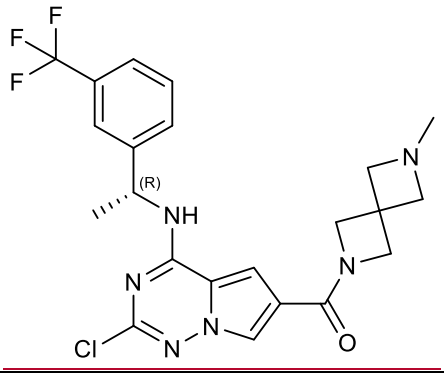
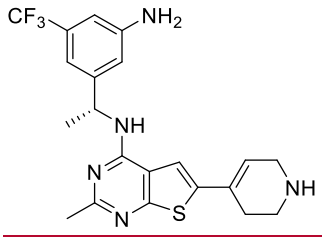
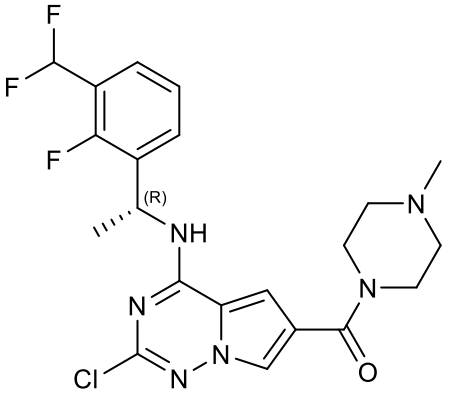
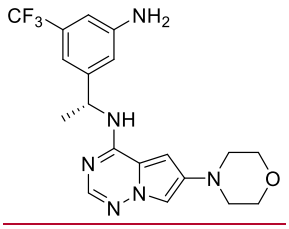
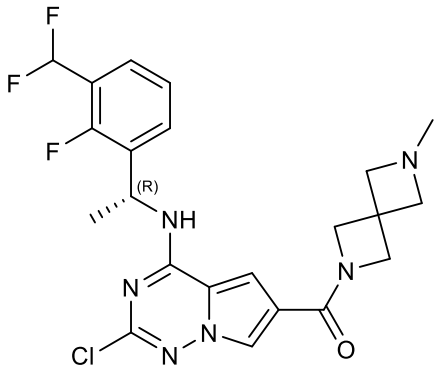
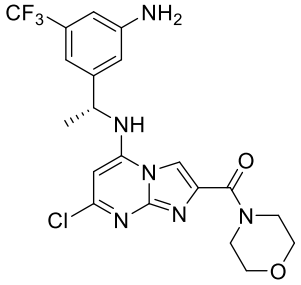
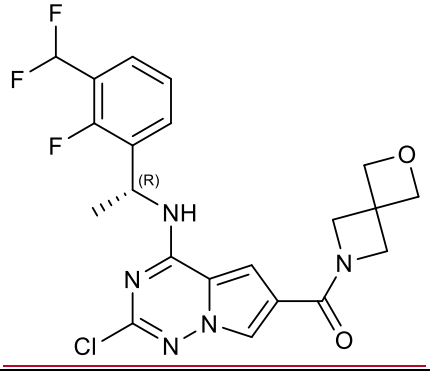
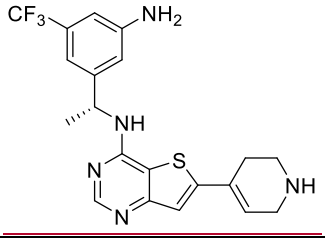
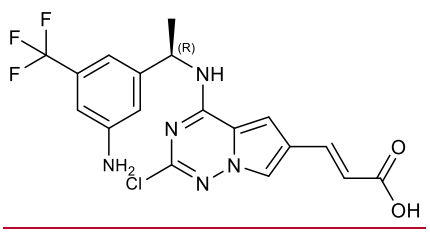
Example 22.		Example 74.	
Example 23.		Example 75.	
Example 24.		Example 76.	
Example 25.		Example 77.	

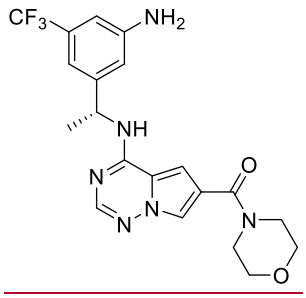
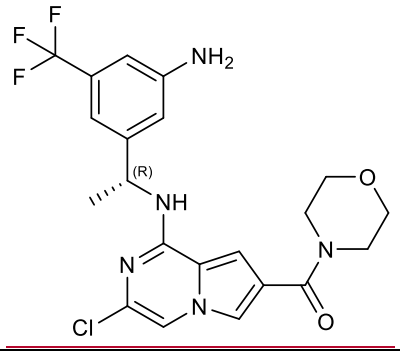
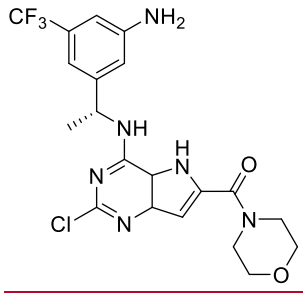
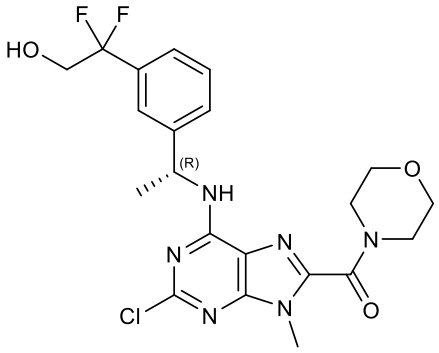
Example 26.		Example 78.	
Example 27.		Example 79.	
Example 28.		Example 80.	
Example 29.		Example 81.	

Example 30.		Example 82.	
Example 31.		Example 83.	
Example 32.		Example 84.	
Example 33.		Example 85.	
Example 34		Example 86.	

Example 35.		Example 87.	
Example 36.		Example 88.	
Example 37.		Example 89.	
Example 38.		Example 90.	
Example 39.		Example 91.	

		Example 92.	
Example 41.		Example 93.	
Example 42.		Example 94.	
Example 43.		Example 95.	
Example 44.		Example 96.	

Example 45.		Example 97.	
Example 46.		Example 98.	
Example 47.		Example 99.	
Example 48.		Example 100.	
Example 49.		Example 101.	

Example 50.		Example 102.	
Example 51.		Example 103.	

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~~26~~19. A pharmaceutical composition comprising a compound of any one of claims 1-~~25~~18, or a pharmaceutically acceptable salt, solvate, stereoisomer, or ~~hydrate,~~ tautomer~~, or isomer~~ thereof, and a pharmaceutically acceptable carrier.

~~27. Use of a compound of any one of claims 1-25, or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or isomer thereof, in the manufacture of a medicament for inhibiting SOS1 in a subject.~~

~~28. Use of a compound of any one of claims 1-25, or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or isomer thereof, in the manufacture of a medicament for inhibiting the interaction of SOS1 and a RAS-family protein in a cell or inhibiting the interaction of SOS1 and RAC1 in a cell.~~

~~29. Use of a compound of any of claims 1-25, or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or isomer thereof, in the manufacture of a medicament for treating or preventing a disease, wherein treating or preventing the disease is characterized by inhibition of the interaction of SOS1 and a RAS-family protein or by inhibition of the interaction of SOS1 and RAC1.~~

~~30~~20. Use of a compound of any of claims 1-~~25~~18, or a pharmaceutically acceptable salt, solvate, ~~hydrate~~stereoisomer, or tautomer~~, or~~ isomer thereof, in the manufacture of a medicament for treating or preventing cancer in a subject in need thereof.

~~31~~21. A compound of any one of claims 1-~~25~~18, or a pharmaceutically acceptable salt, solvate, stereoisomer, or ~~hydrate,~~ tautomer~~, or isomer~~ thereof, for use in inhibiting SOS1 in a subject, or for use in inhibiting the interaction of SOS1 and a RAS-family protein in a cell or inhibiting the interaction of SOS1 and RAC1 in a cell, or for use in treating or preventing a disease, wherein treating or preventing the disease is characterized by inhibition of the interaction of SOS1 and a RAS-family protein or by inhibition of the interaction of SOS1 and RAC1, or for use in treating or preventing cancer in a subject in need thereof.

~~32~~22. The use of claim 20~~29 or 30~~, or the compound for use of claim ~~31~~21, wherein the disease or cancer is selected from the group consisting of pancreatic cancer, lung cancer, colorectal cancer, hematological cancer, cholangiocarcinoma, multiple myeloma, melanoma, uterine cancer, endometrial cancer, thyroid cancer, acute myeloid leukemia, bladder cancer, urothelial cancer, gastric cancer, cervical cancer, head and neck squamous cell carcinoma, diffuse large B cell lymphoma, esophageal cancer, chronic lymphocytic leukemia, hepatocellular cancer, breast cancer, ovarian cancer, prostate cancer, glioblastoma, renal cancer and sarcomas.

~~33~~23. The use of claim 20~~29~~, or the compound for use of claim ~~31~~21, wherein the disease is a RASopathy.

~~34~~24. The use or compound for use of claim ~~33~~23, wherein the RASopathy is selected from the group consisting of Neurofibromatosis type 1 (NF1), Noonan Syndrome (NS), Noonan Syndrome with Multiple Lentigines (NSML), ~~-~~Capillary Malformation-Arteriovenous Malformation Syndrome (CM-AVM), Costello Syndrome (CS), Cardio-Facio-Cutaneous Syndrome (CFC), Legius Syndrome, and Hereditary gingival fibromatosis.