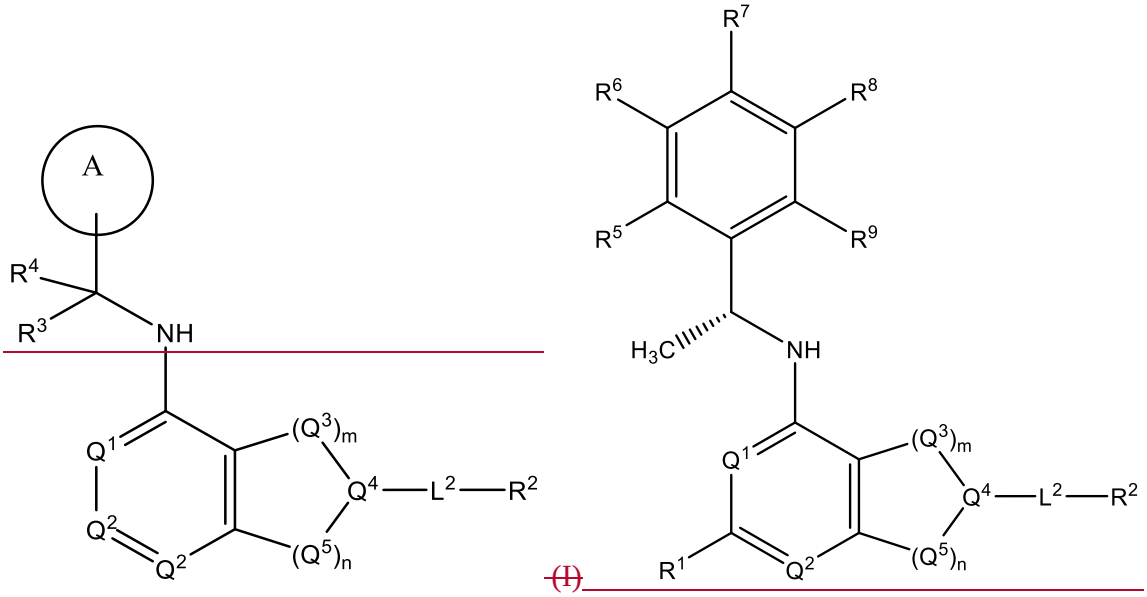
Natl. Acad. Sci. 2014, 111(9):3401-6). However, binding of these molecules seems to lead to increased nucleotide exchange and thereby activation of RAS instead of deactivation.

[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 is ~~CH or~~ N;

Q2 is N;

Q^4 is ~~CH, C, or~~ N;

~~each Q^2 is independently C-R^1 or N, wherein one Q^2 is N and the other Q^2 is C-R^1;~~

each Q^3 and Q^5 are independently $C(R^{QC})_2$, NR^{QN}, CO, O, S, or SO_2, wherein each R^{QC} is independently H, F, Cl, Br, or 6-10 membered aryl, and wherein each R^{QN} is independently H, C_{1-6} alkyl, or 6-10 membered aryl;

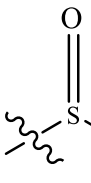
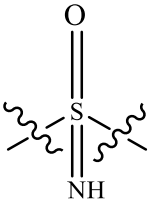
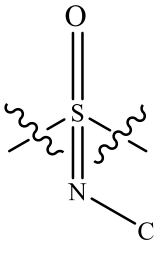
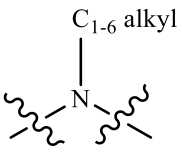
~~wherein at least one of Q^1, Q^2, Q^3, Q^4, and Q^5 is N, NR^{QN}, O, or SO_2;~~

m is 0, 1, 2, or 3;

n is 0, 1, 2, or 3;

wherein when m is 0, then n is not 0;

R^1 is selected from the group consisting of H, C_{1-6} alkyl, halogen, -$CONHR^{1a}$, -NHR^{1a}, –OR^{1a}, cyclopropyl, azetidinyl, and –CN; wherein each C_{1-6} alkyl and azetidinyl is optionally substituted with halogen, R^{1a}, -NHR^{1a}, or –OR^{1a}; wherein R^{1a} is H, C_{1-6} alkyl, cyclopropyl, 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, -$NR^{2b}R^{2c}$, -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, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} methoxyalkyl, –OH, –OR^{2a}, oxo, =N, halogen,

–C(O)R^{2a}, –C(O)OR^{2a}, –C(O)N$R^{2b}R^{2c}$, -SO_2R^{2a}, –CN, -N$R^{2b}R^{2c}$, 3-6 membered cycloalkyl, 3-7 membered heterocyclyl, 6-10 membered aryl, or 5-10 membered heteroaryl;

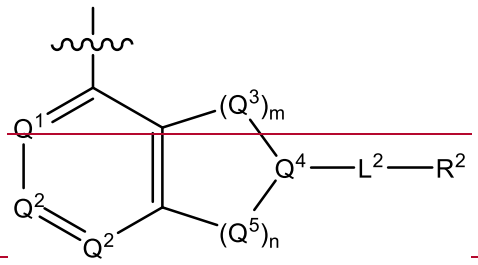
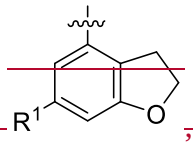
wherein R^{2a} is H, C_{1-6} alkyl, C_{1-6} haloalkyl, 3-7 membered heterocyclyl, or –$(CH_2)_rOCH_3$, wherein r is 1, 2, or 3;

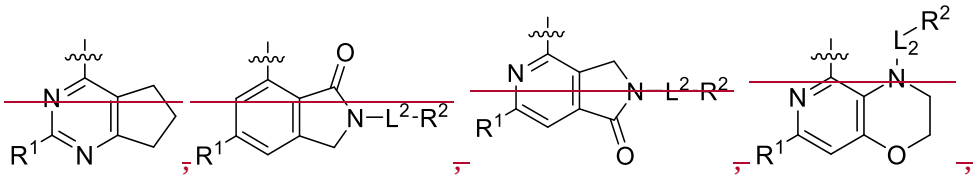
wherein R^{2b} is H or C_{1-6} alkyl;

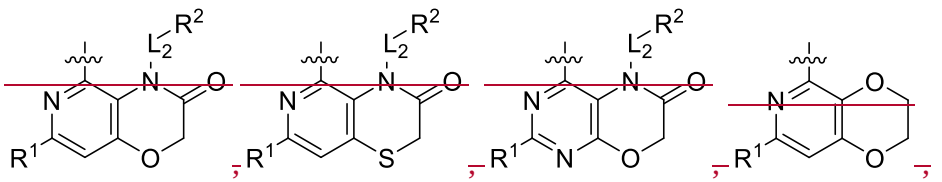
wherein R^{2c} is H or C_{1-6} alkyl;

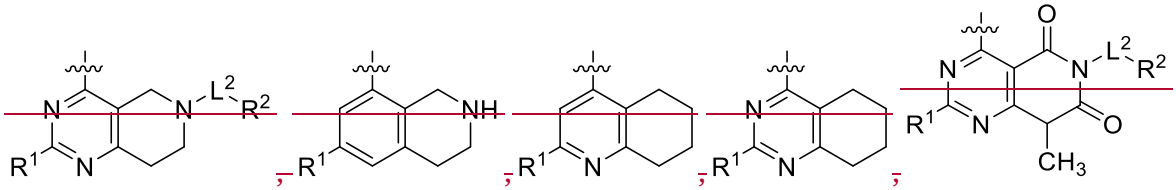
~~R^3 and R^4 are independently H or C_{1-6} alkyl optionally substituted with halo or -OH; wherein at least one of R^3 and R^4 is H or wherein R^3 and R^4 together with the atom to which they are attached combine to form a 3-6 membered cycloalkyl; and~~

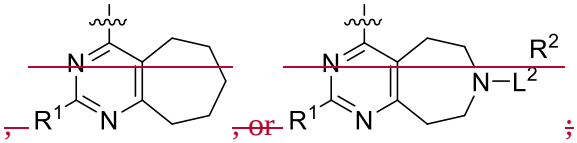
~~A is an optionally substituted 6-membered aryl or an optionally substituted 5-6 membered heteroaryl;~~

~~with the proviso that when~~  ~~is~~ ;





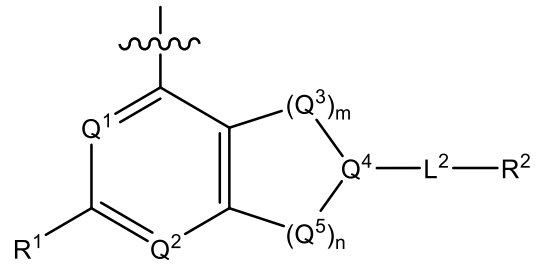
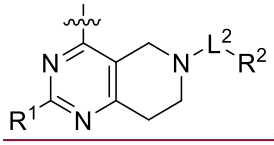
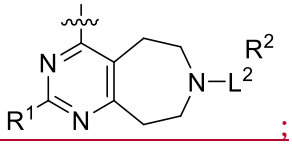




R^5, R^6, R^7, R^8, and R^9 are independently selected from the group consisting of H, D, C_{1-6} alkyl, C_{2-6} alkenyl, 4-8 membered cycloalkenyl, C_{2-6} alkynyl, 3-8 membered cycloalkyl, 3-14 membered heterocyclyl, -OH, halogen, $–NO_2$, –CN, $–NR^{11}R^{12}$, $–SR^{10}$, $–S(O)_2NR^{11}R^{12}$, $–S(O)_2R^{10}$, $–NR^{10}S(O)_2NR^{11}R^{12}$, $–NR^{10}S(O)_2R^{11}$, $–S(O)NR^{11}R^{12}$, $–S(O)R^{10}$, $–NR^{10}S(O)NR^{11}R^{12}$, $–NR^{10}S(O)R^{11}$, $–C(O)R^{10}$, and $–CO_2R^{10}$, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, 4-8 membered cycloalkenyl, C_{2-6} alkynyl, 3-8 membered cycloalkyl, and 3-14 membered heterocyclyl are independently optionally substituted with –OH, halogen, $–NO_2$, oxo, –CN, $–R^{10}$, $–OR^{10}$, $–NR^{11}R^{12}$, $–SR^{10}$, $–S(O)_2NR^{11}R^{12}$, $–S(O)_2R^{10}$, $–NR^{10}S(O)_2NR^{11}R^{12}$, $–NR^{10}S(O)_2R^{11}$, $–S(O)NR^{11}R^{12}$, $–S(O)R^{10}$, $–NR^{10}S(O)NR^{11}R^{12}$, $–NR^{10}S(O)R^{11}$, 3-8 membered cycloalkyl, 3-14 membered heterocyclyl, 6-10 membered aryl, or 5-10 membered heteroaryl, or any two adjacent R^5, R^6, R^7, R^8, and R^9 form a 3-14 membered fused ring;

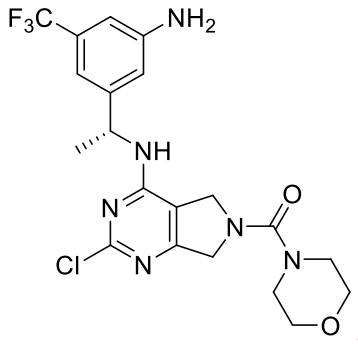
R^{10}, R^{11}, and R^{12} are at each occurrence independently selected from H, D, C_{1-6} alkyl, C_{2-6} alkenyl, 4-8 membered cycloalkenyl, C_{2-6} alkynyl, 3-8 membered cycloalkyl, 3-14 membered heterocyclyl, $–OR^{13}$, $–SR^{13}$, halogen, $–NR^{13}R^{14}$, $–NO_2$, and –CN; and

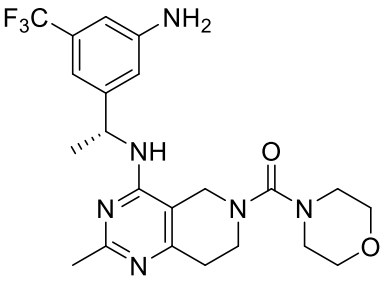
R^{13} and R^{14} are at each occurrence independently selected from H, D, C_{1-6} alkyl, C_{2-6} alkenyl, 4-8 membered cycloalkenyl, C_{2-6} alkynyl, 3-8 membered cycloalkyl, and 3-14 membered heterocyclyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, 4-8 membered cycloalkenyl, C_{2-6} alkynyl, 3-8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

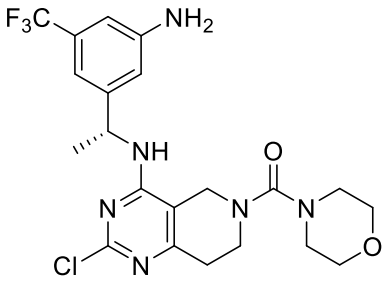
with the proviso that when  is  , or  ;

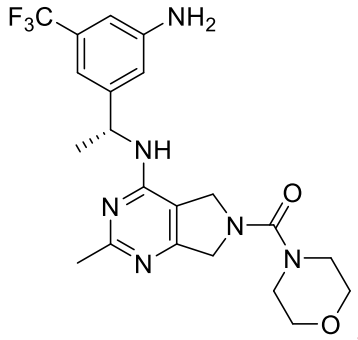
then R^1 is not H.

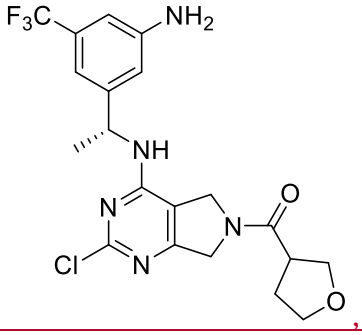
[0011b] In another aspect of the present disclosure, there is provided a compound, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, selected from the group consisting of the following compounds:

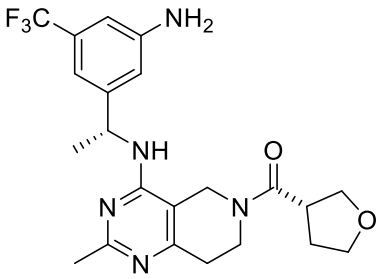


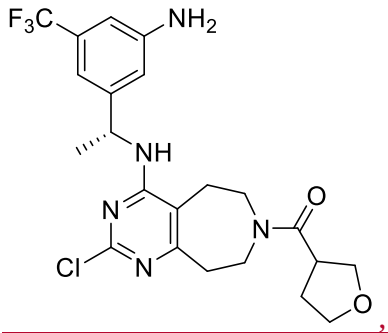
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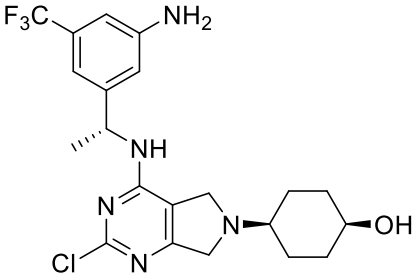
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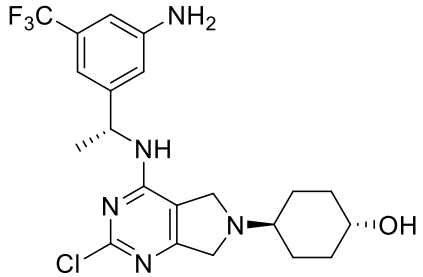
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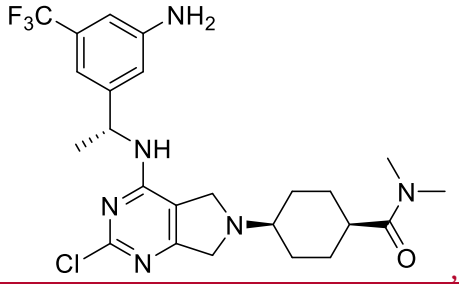
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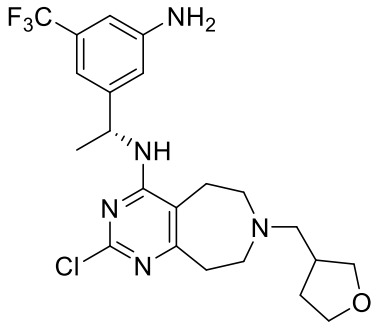
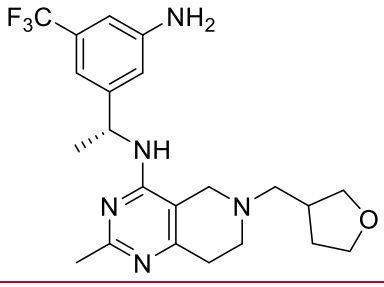
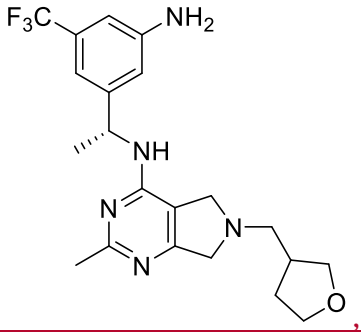
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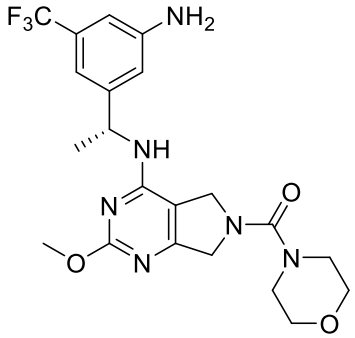
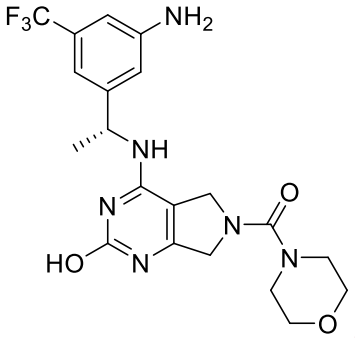
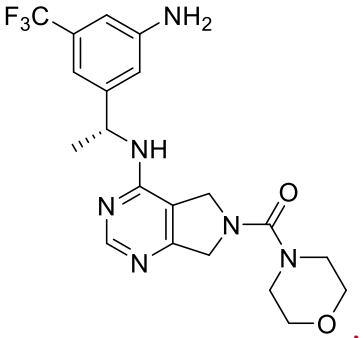
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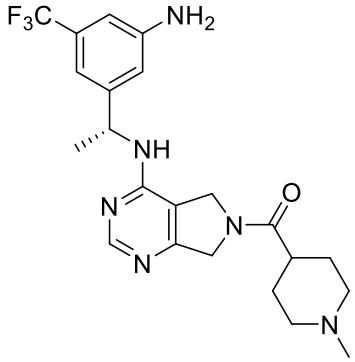
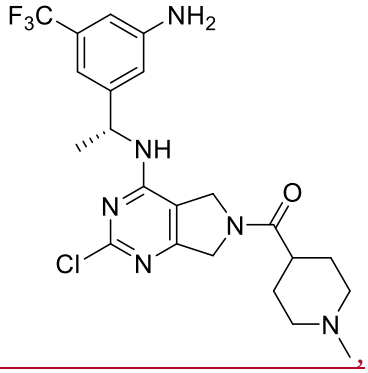
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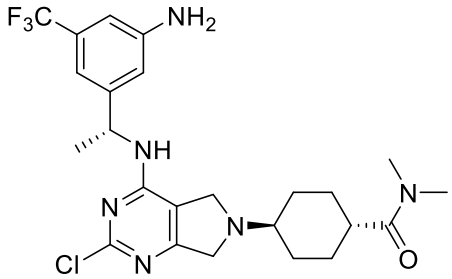
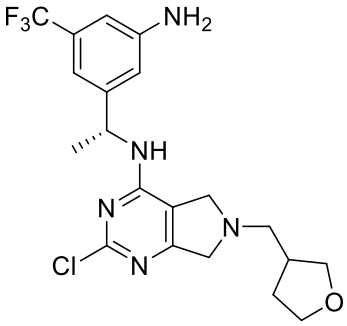
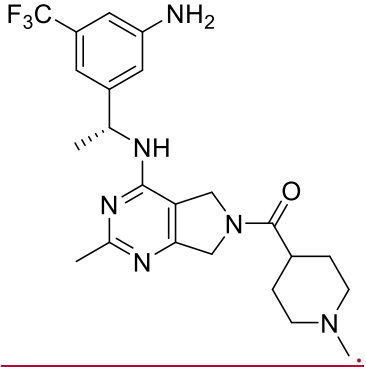
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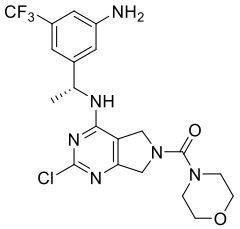
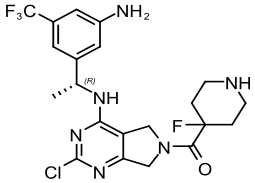
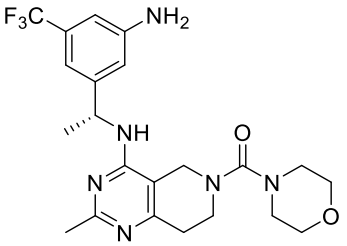
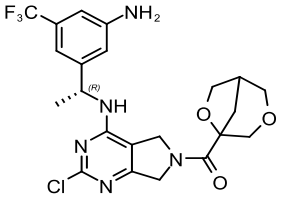
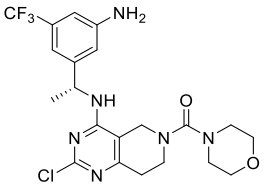
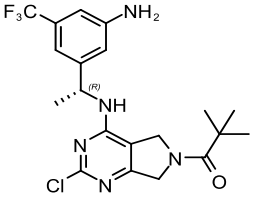
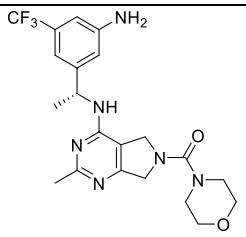
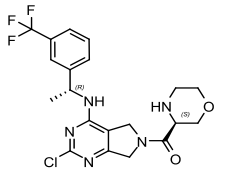
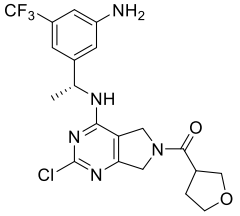
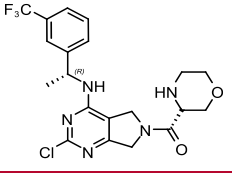
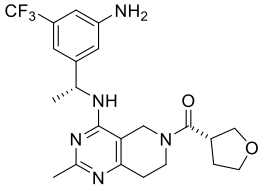
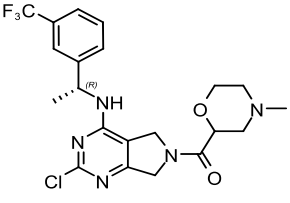

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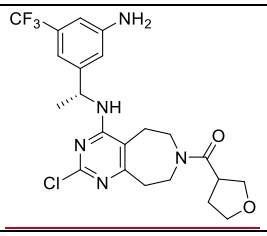
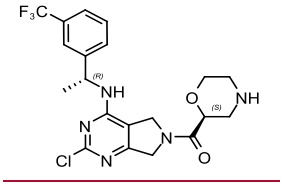
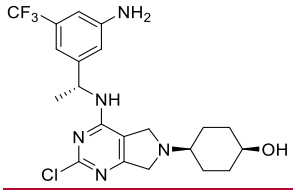
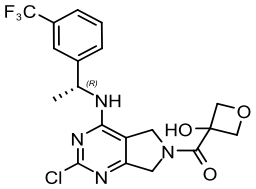
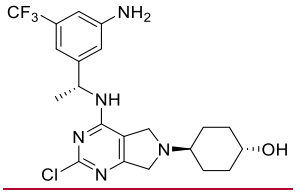
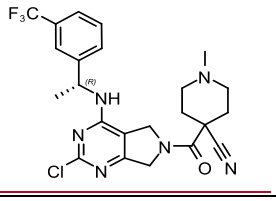
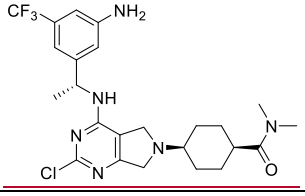
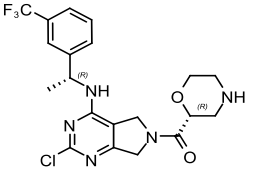
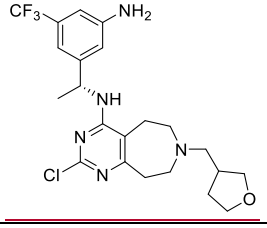
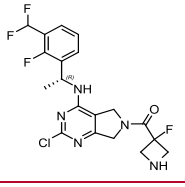
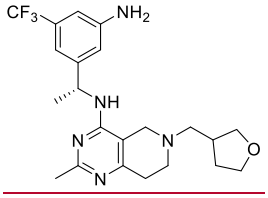
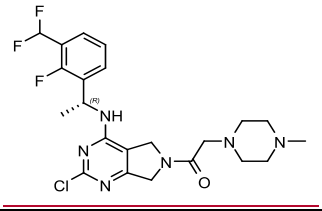
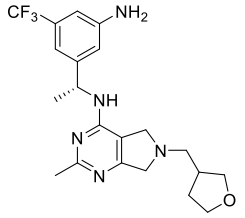
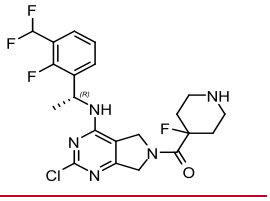
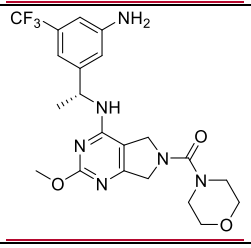
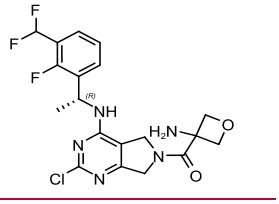

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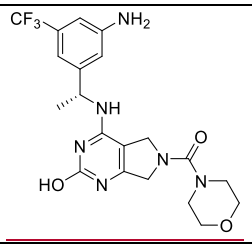
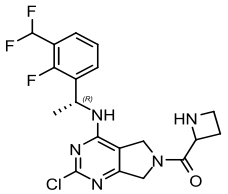
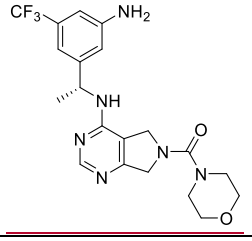
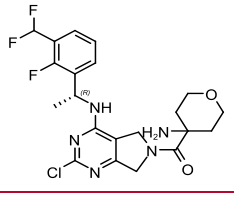
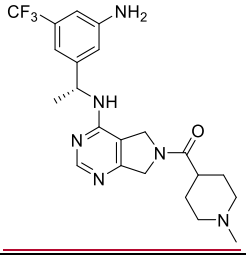
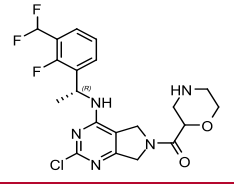
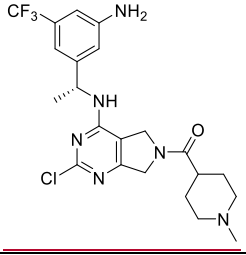
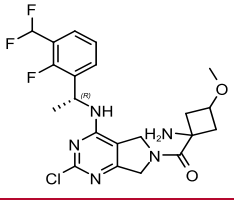
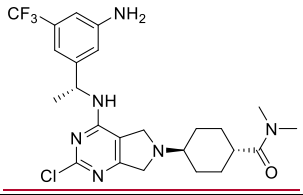
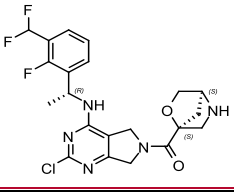
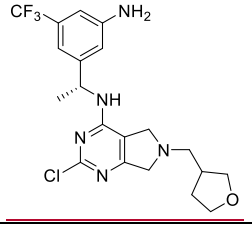
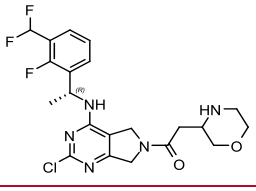
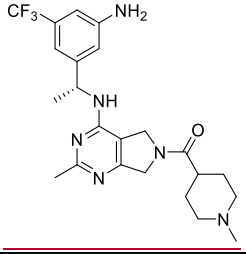
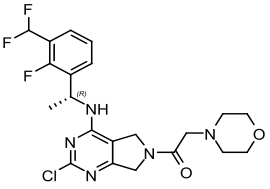
[0011c] In a further aspect of the present disclosure, there is provided a compound, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, selected from the group consisting of compounds shown in the following table

Example #	Structure	Example #	Structure
Example 1.		Example 272.	
Example 2.		Example 273.	
Example 3.		Example 274.	
Example 4.		Example 275.	
Example 5.		Example 276.	
Example 6.		Example 277.	

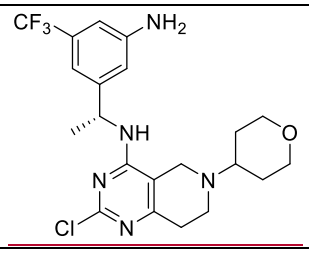
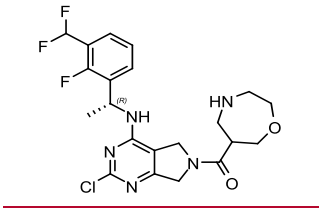
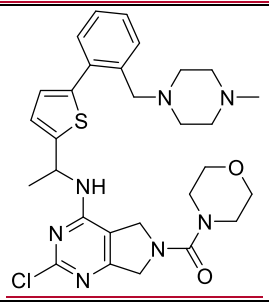
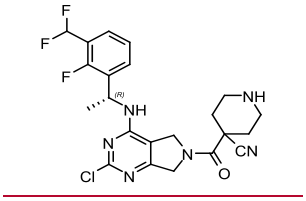
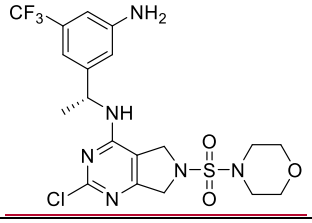
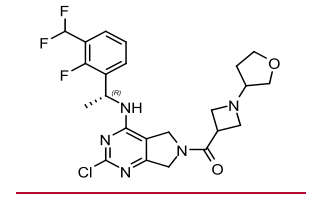
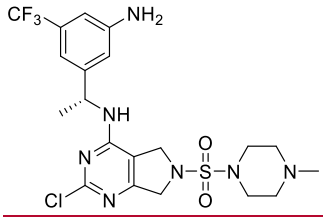
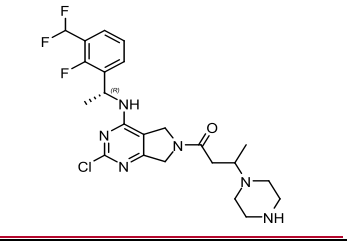
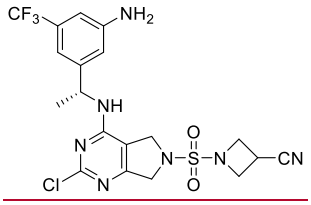
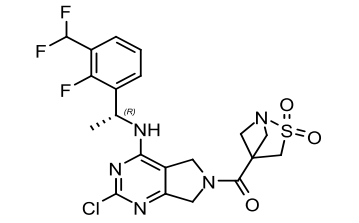
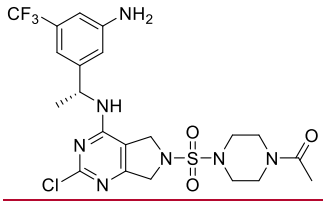
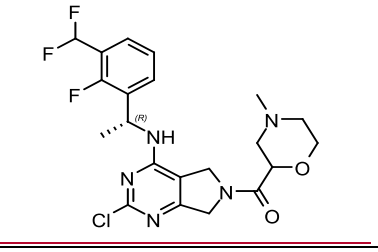
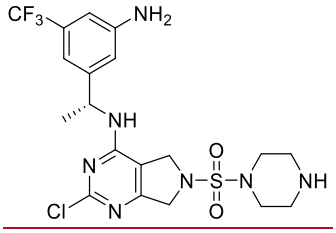
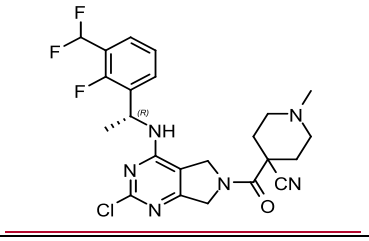
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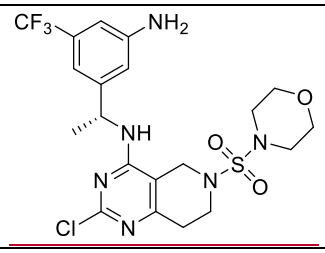
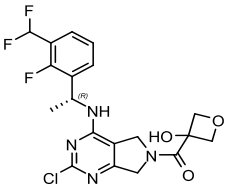
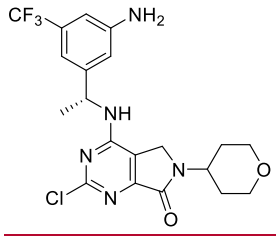
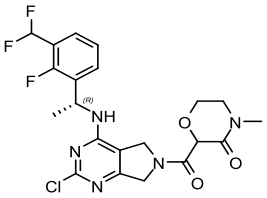
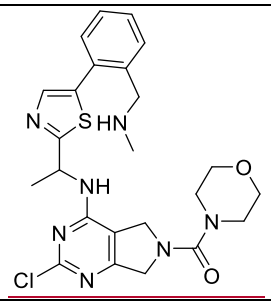
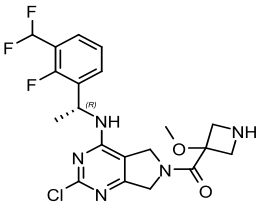
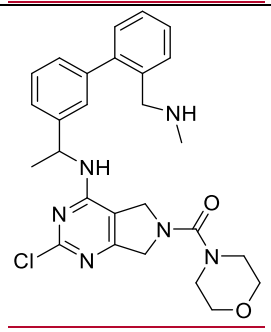
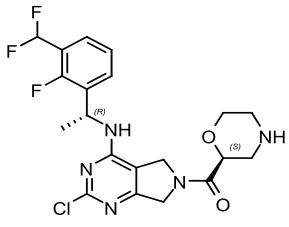
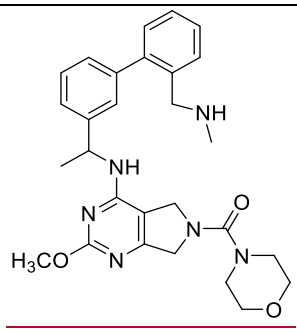
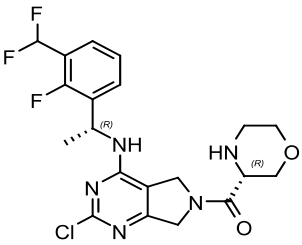
Example 7.		Example 278.	
Example 8.		Example 279.	
Example 9.		Example 280.	
Example 10.		Example 281.	
Example 11.		Example 282.	
Example 12.		Example 283.	
Example 13.		Example 284.	
Example 14.		Example 285.	

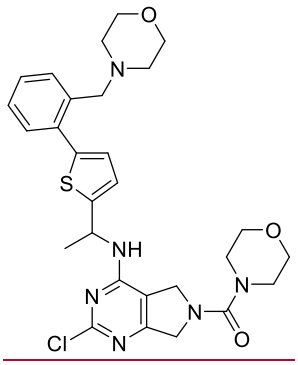
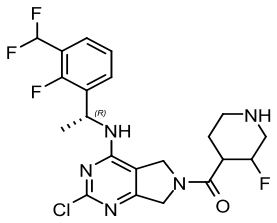
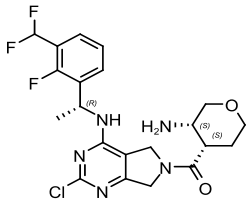
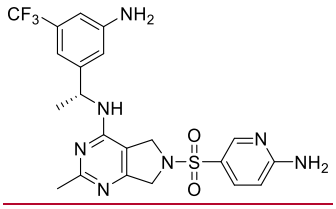
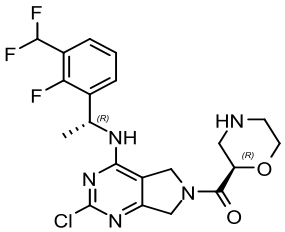
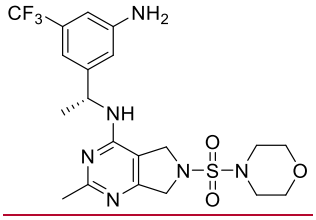
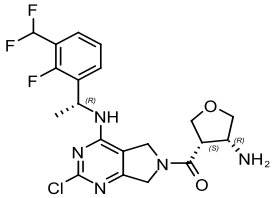
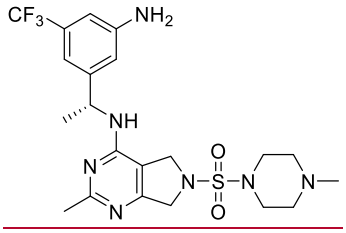
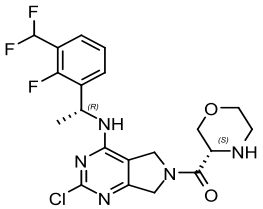
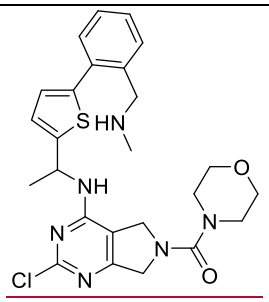
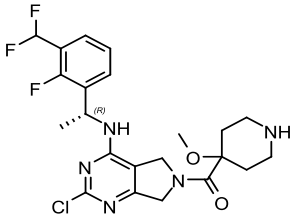
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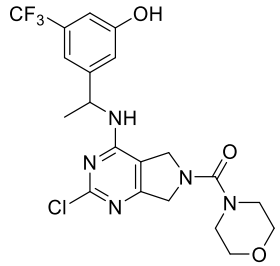
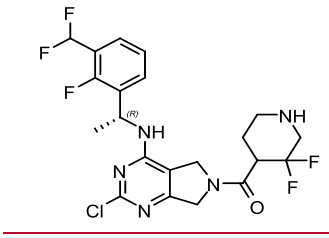
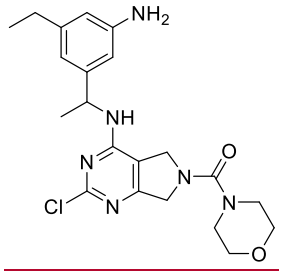
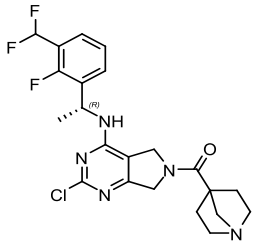
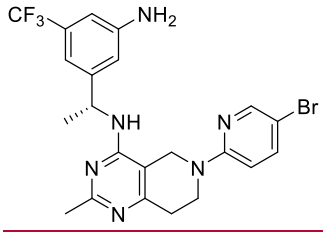
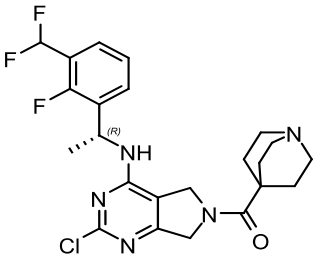
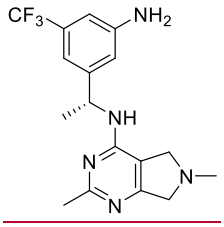
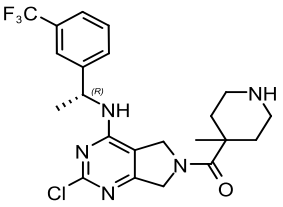
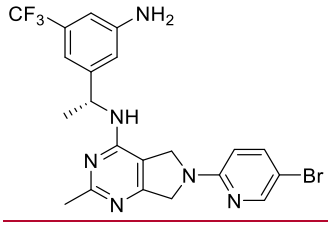
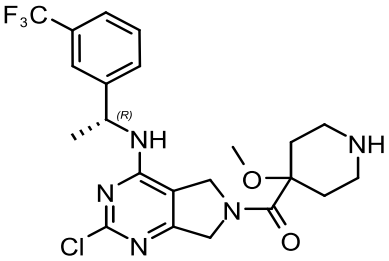
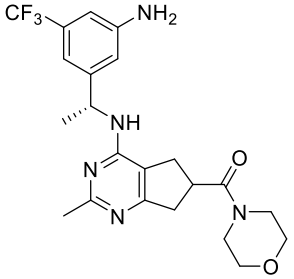
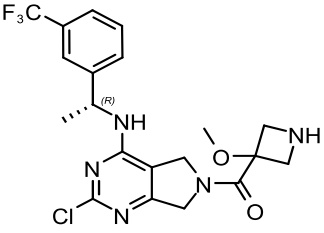
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Example 18.		Example 289.	
Example 19.		Example 290.	
Example 20.		Example 291.	
Example 21.		Example 292.	

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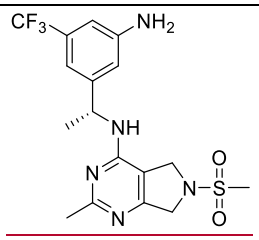
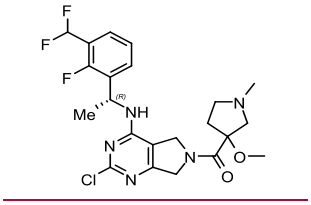
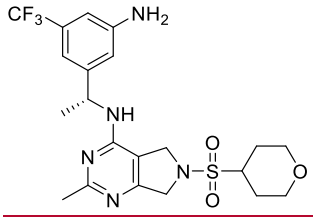
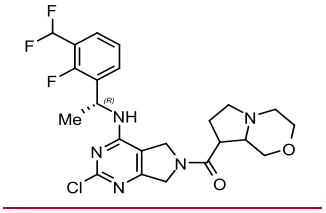
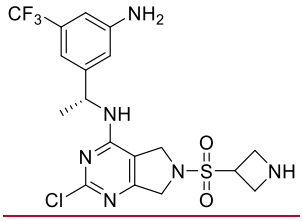
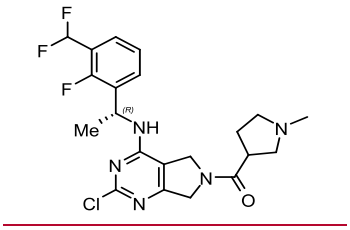
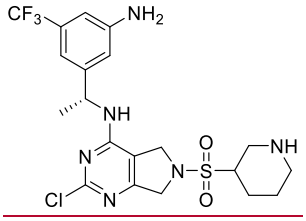
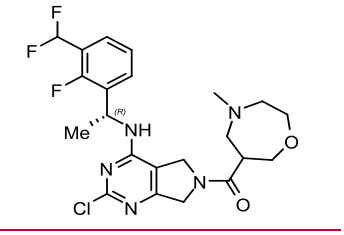
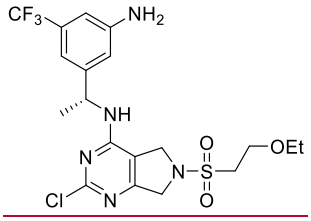
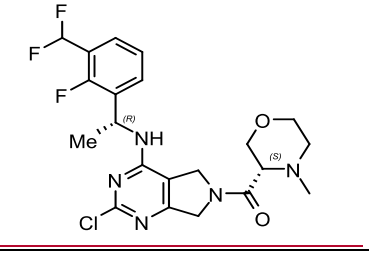
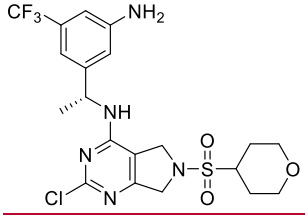
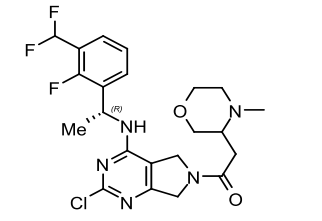
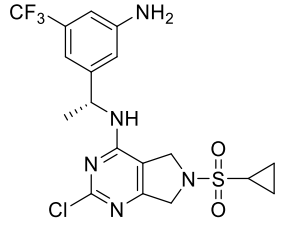
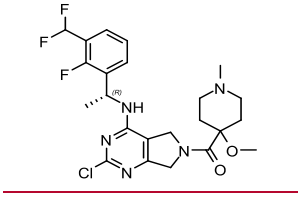
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Example 26.		Example 297.	
Example 27.		Example 298.	
Example 28.		Example 299.	

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Example 30.		Example 301.	
Example 31.		Example 302.	
Example 32.		Example 303.	
Example 33.		Example 304.	

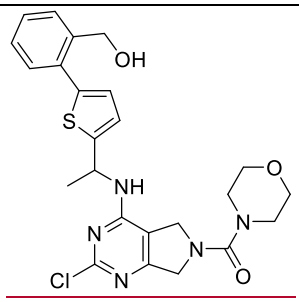
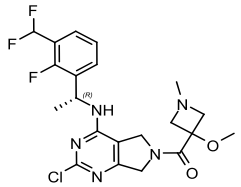
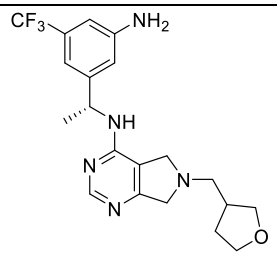
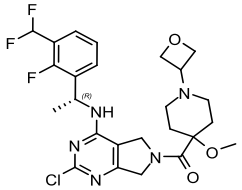
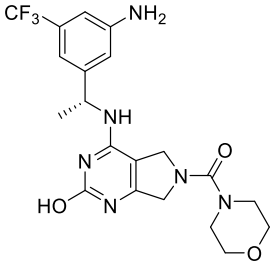
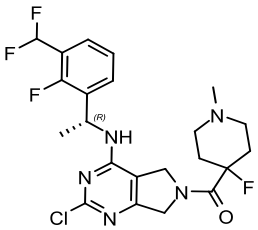
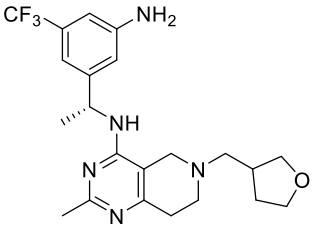
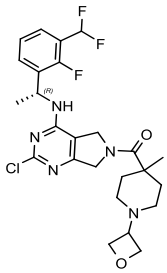
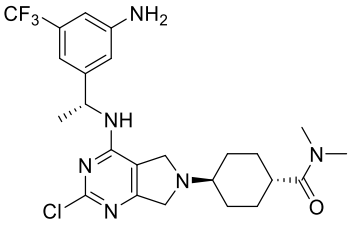
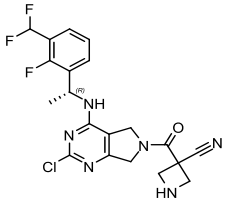
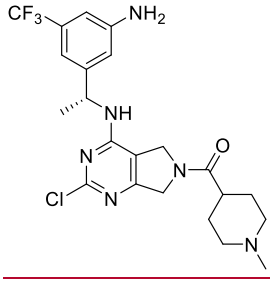
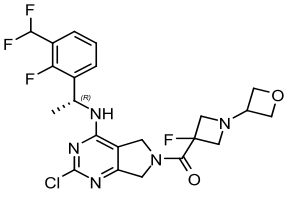
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Example 38.		Example 309.	
Example 39.		Example 310.	

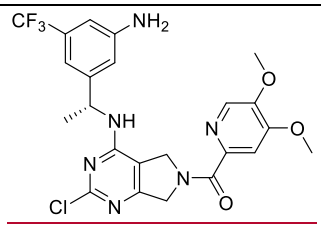
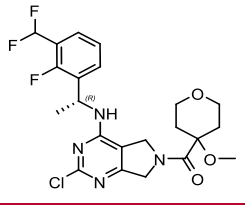
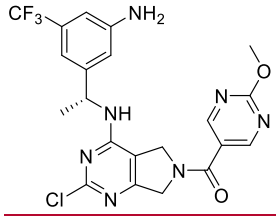
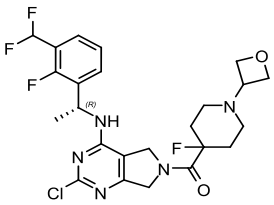
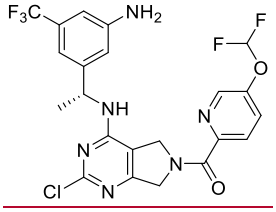
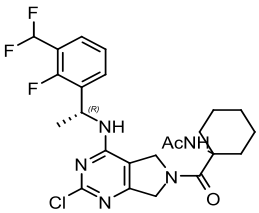
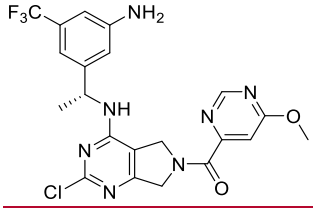
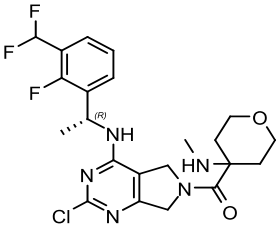
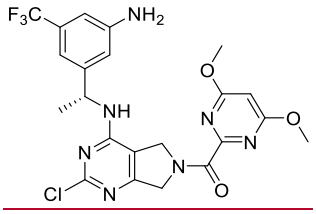
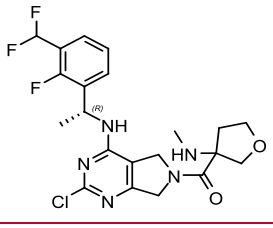
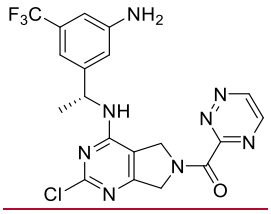
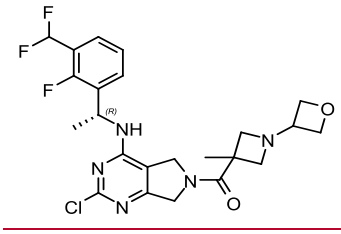
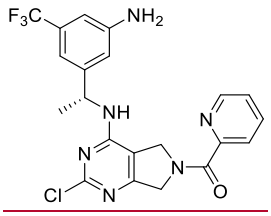
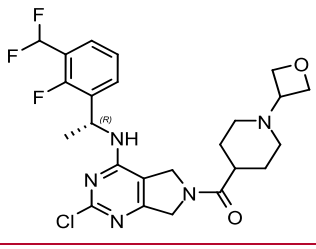
Example 40.		Example 311.	
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Example 43.		Example 314.	
Example 44.		Example 315.	
Example 45.		Example 316.	

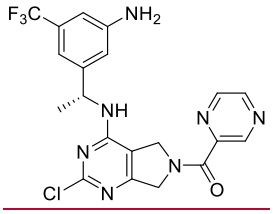
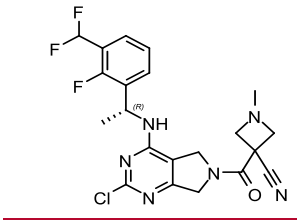
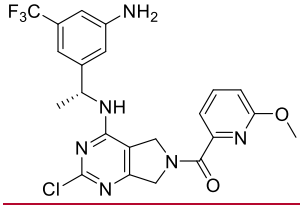
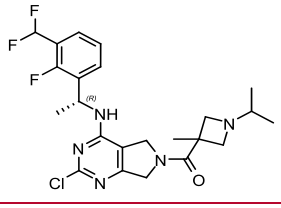
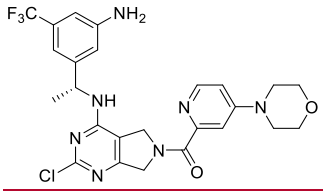
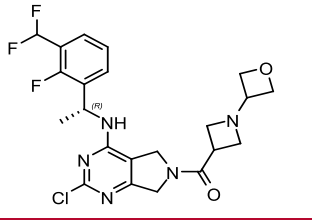
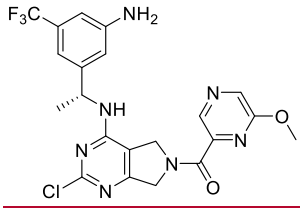
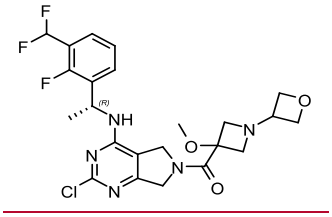
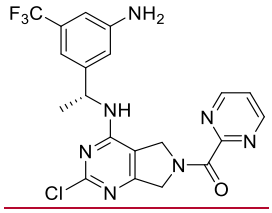
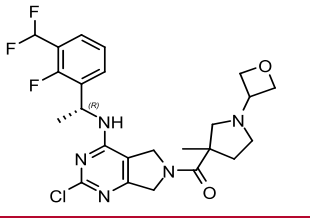
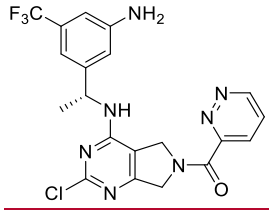
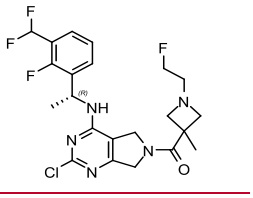
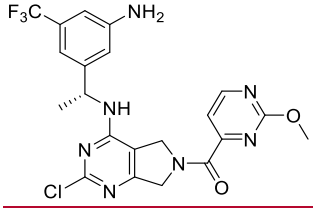
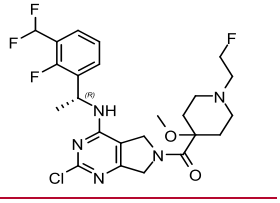
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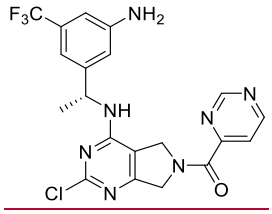
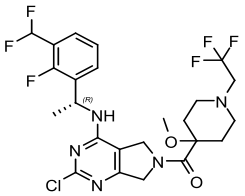
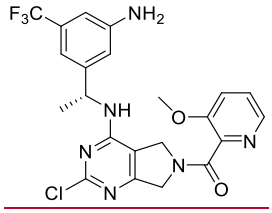
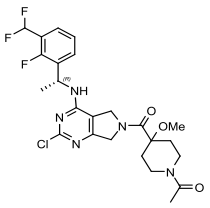
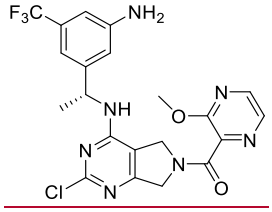
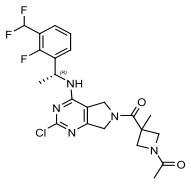
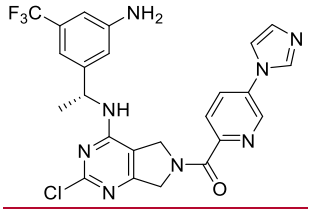
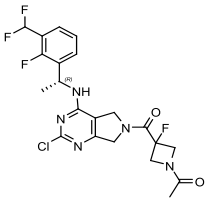
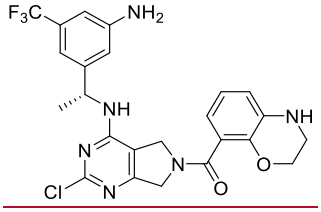
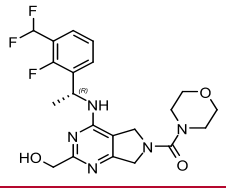
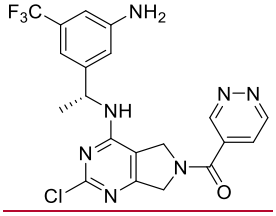
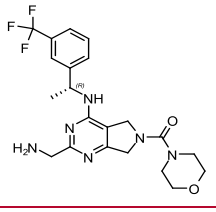
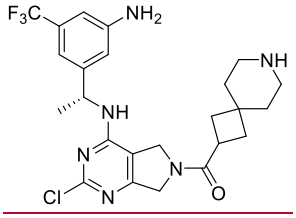
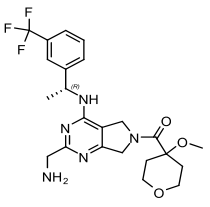
Example 46.		Example 317.	
Example 47.		Example 318.	
Example 48., 166.		Example 319.	
Example 49.		Example 320.	
Example 50.		Example 321.	
Example 51.		Example 322.	
Example 52.		Example 323.	

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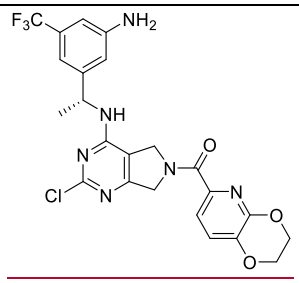
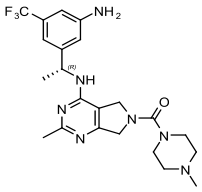
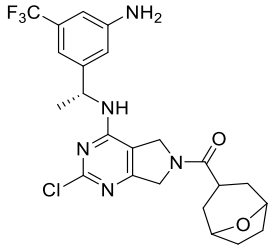
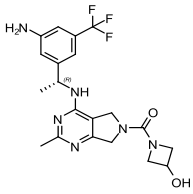
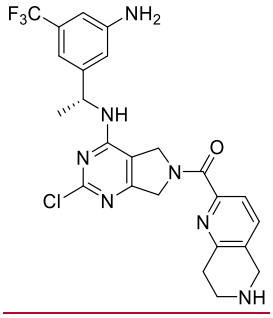
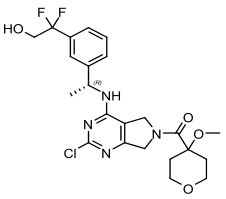
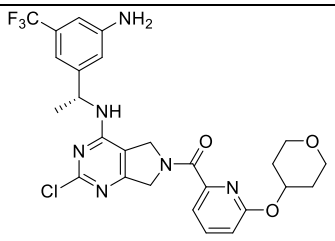
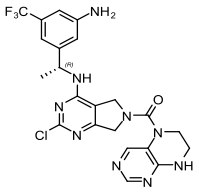
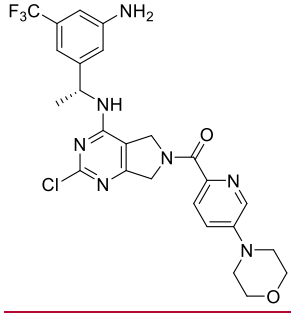
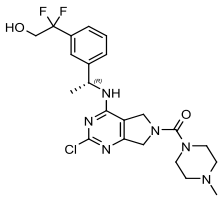
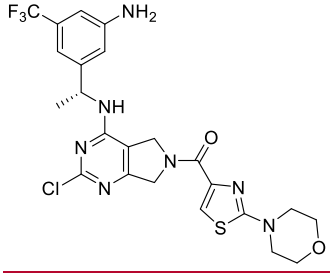
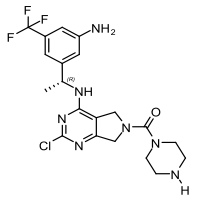
Example 53.		Example 324.	
Example 54., 110.		Example 325.	
Example 55.		Example 326.	
Example 56.		Example 327.	
Example 57.		Example 328.	
Example 58.		Example 329.	

Example 59.		Example 330.	
Example 60.		Example 331.	
Example 61.		Example 332.	
Example 62.		Example 333.	
Example 63.		Example 334.	
Example 64.		Example 335.	
Example 65.		Example 336.	

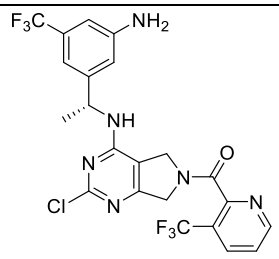
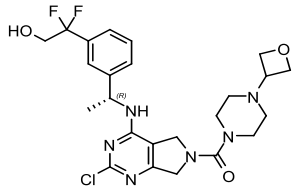
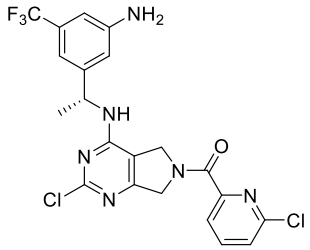
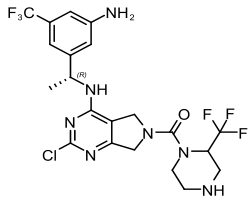
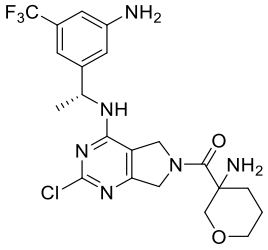
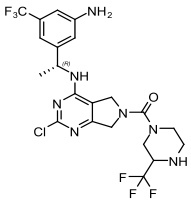
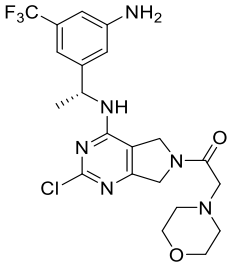
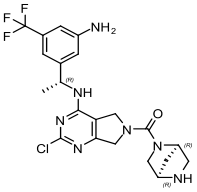
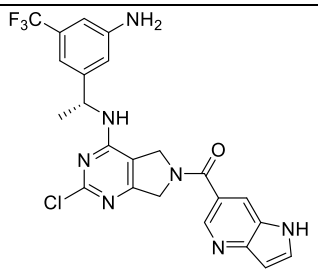
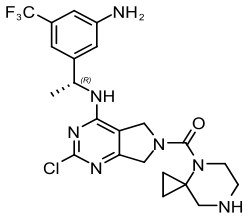
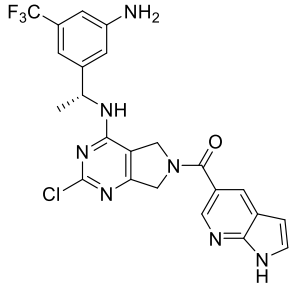
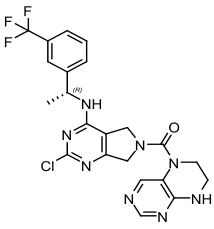
Example 66.		Example 337.	
Example 67.		Example 338.	
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Example 69.		Example 340.	
Example 70.		Example 341.	
Example 71.		Example 342.	
Example 72.		Example 343.	

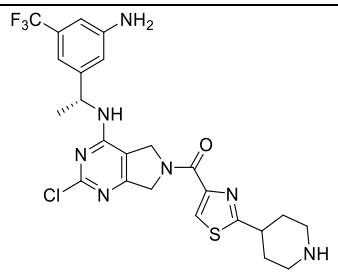
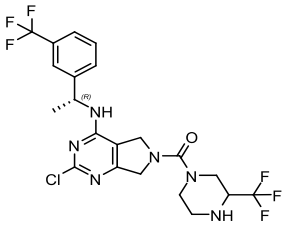
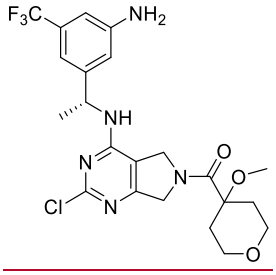
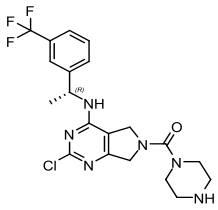
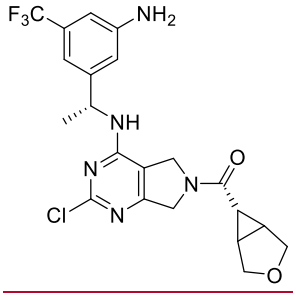
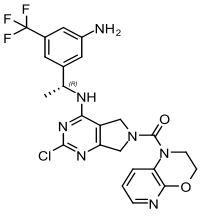
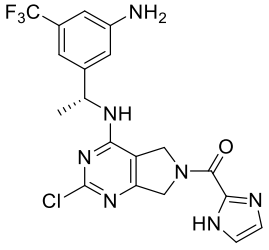
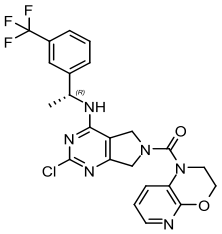
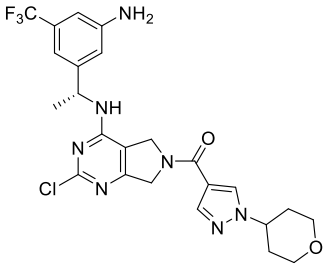
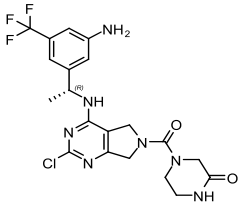
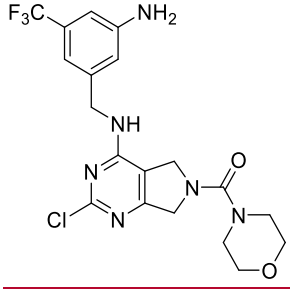
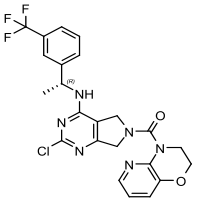
Example 73.		Example 344.	
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Example 76.		Example 347.	
Example 77.		Example 348.	
Example 78.		Example 349.	
Example 79.		Example 350.	

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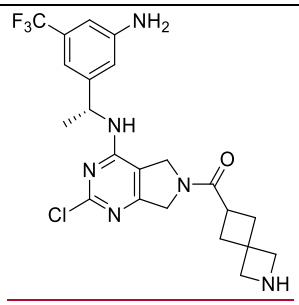
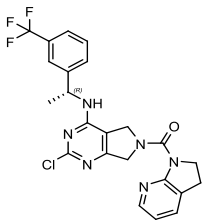
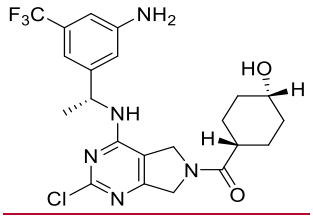
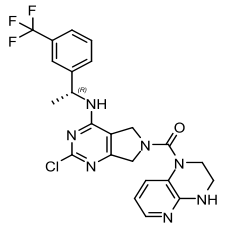
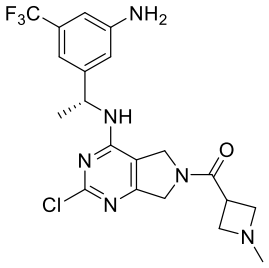
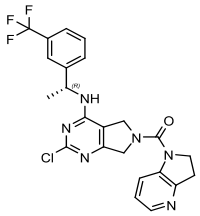
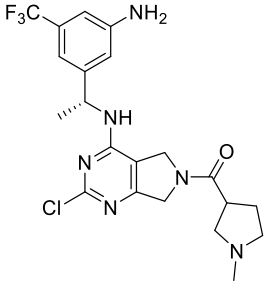
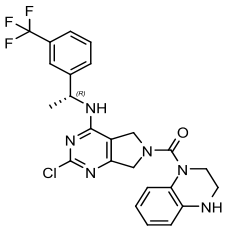
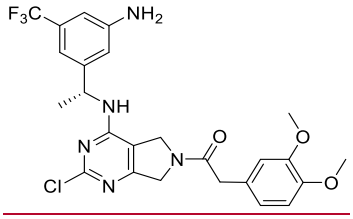
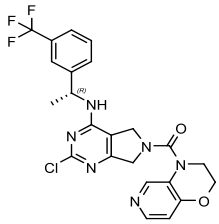
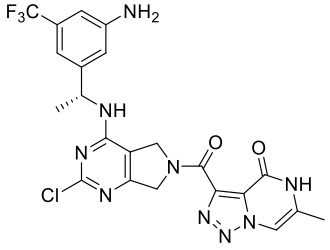
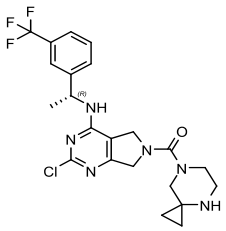
Example 80.		Example 351.	
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Example 82.		Example 353.	
Example 83.		Example 354.	
Example 84.		Example 355.	
Example 85.		Example 356.	

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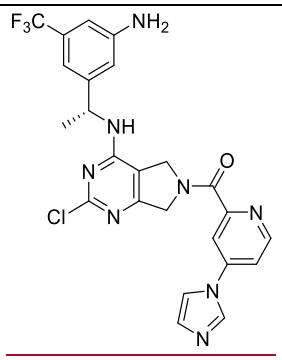
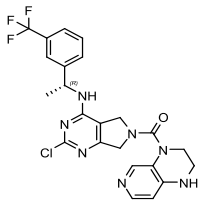
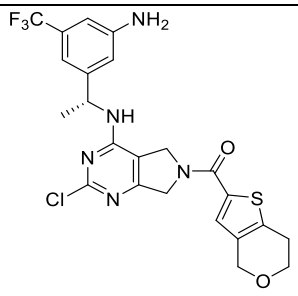
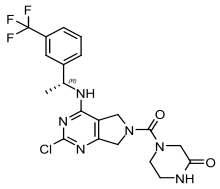
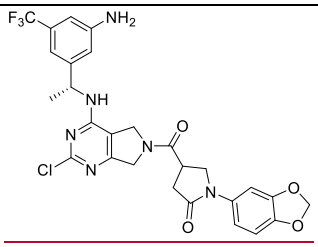
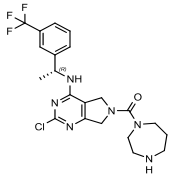
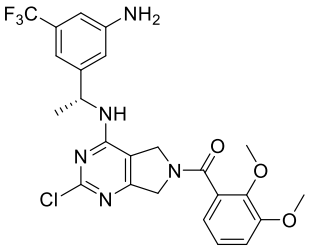
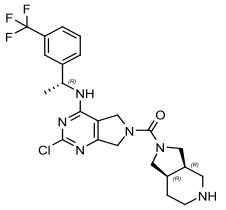
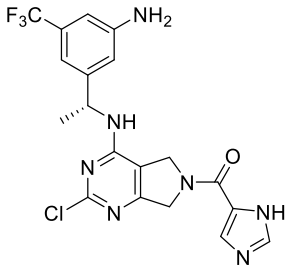
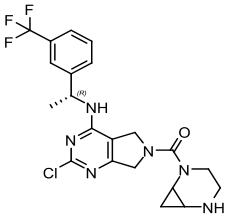
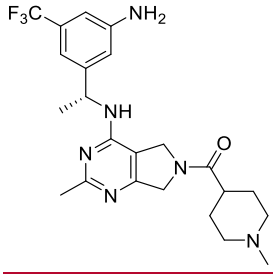
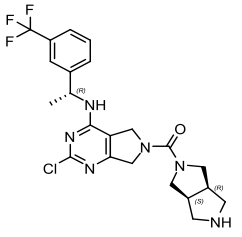
Example 86.		Example 357.	
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Example 89.		Example 360.	
Example 90.		Example 361.	
Example 91.		Example 362.	

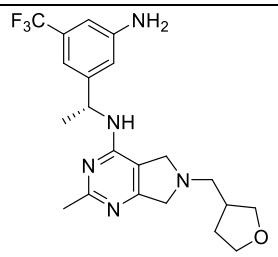
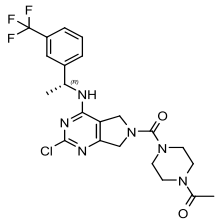
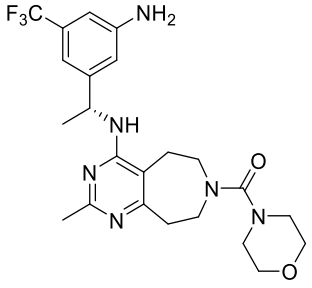
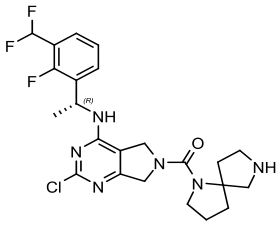
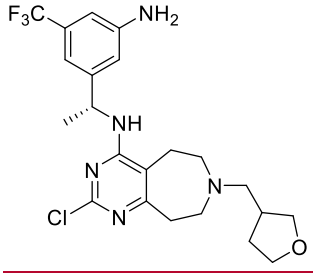
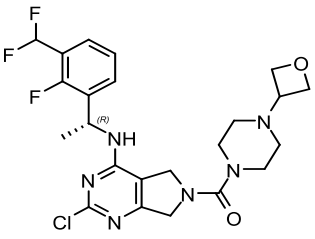
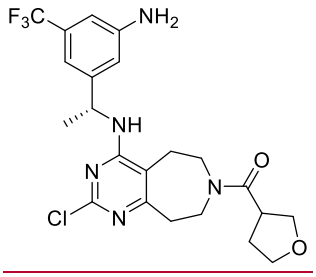
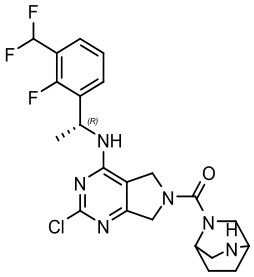
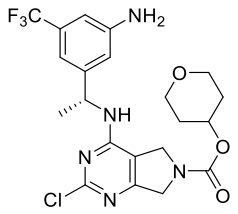
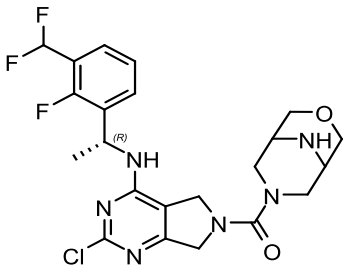
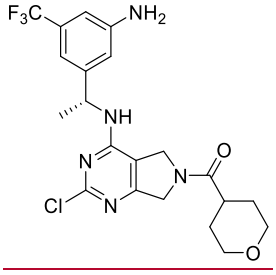
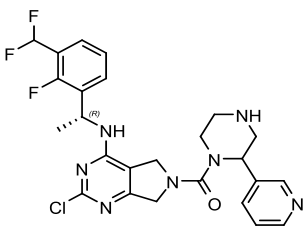
Example 92.		Example 363.	
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Example 94.		Example 365.	
Example 95.		Example 366.	
Example 96.		Example 367.	
Example 97.		Example 368.	

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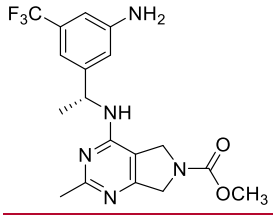
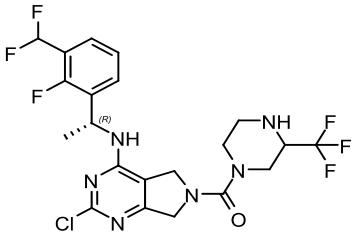
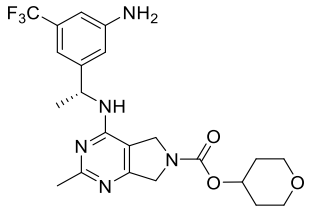
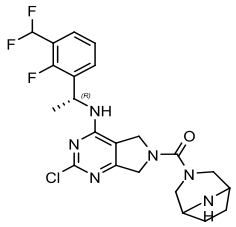
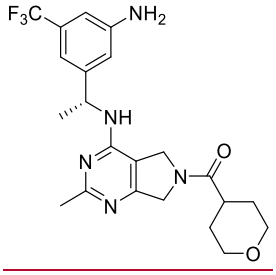
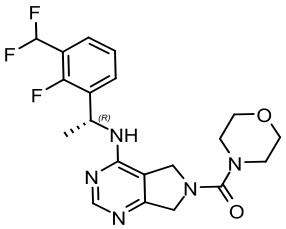
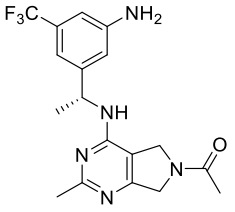
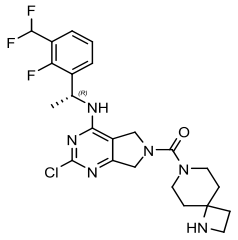
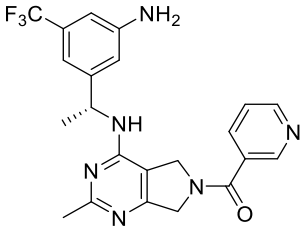
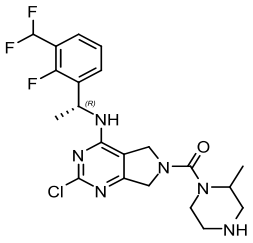
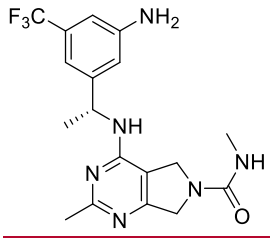
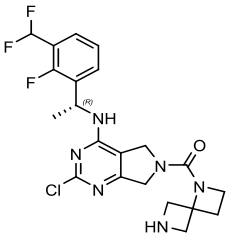
Example 98.		Example 369.	
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Example 100.		Example 371.	
Example 101.		Example 372.	
Example 102.		Example 373.	
Example 103.		Example 374.	

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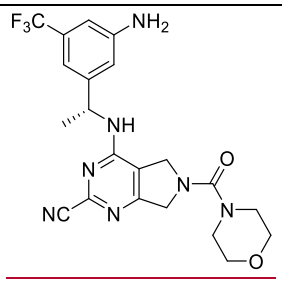
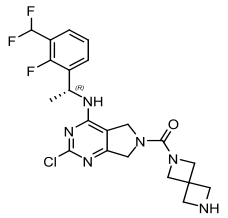
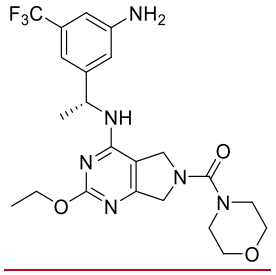
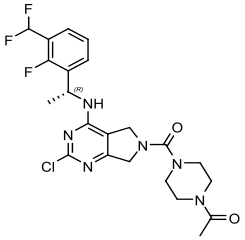
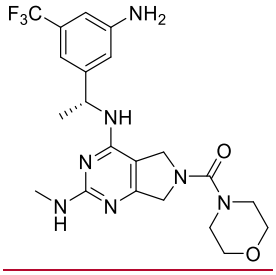
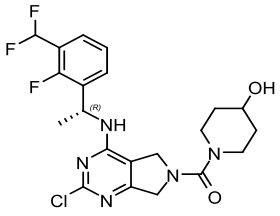
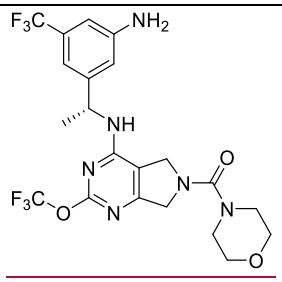
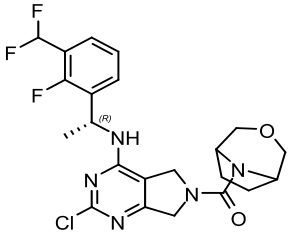
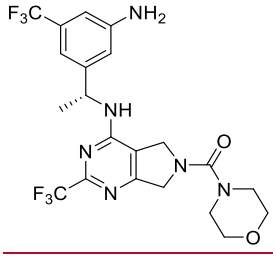
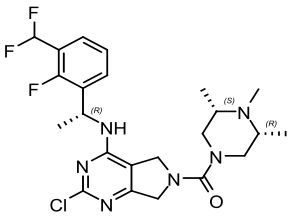
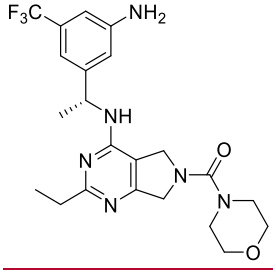
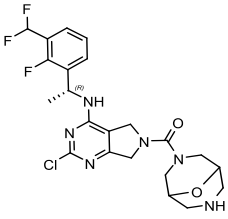
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Example 107.		Example 378.	
Example 108.		Example 379.	
Example 109.		Example 380.	

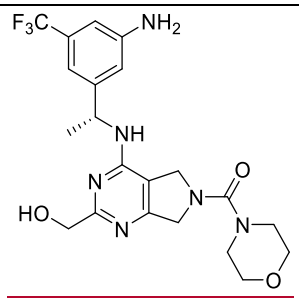
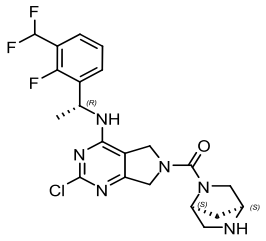
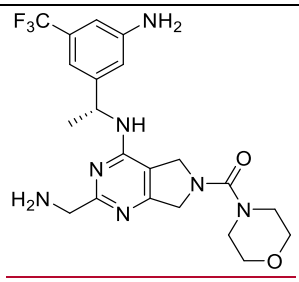
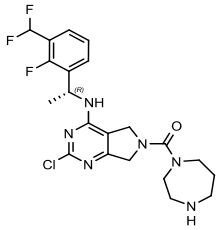
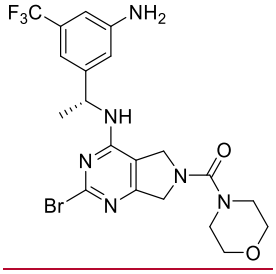
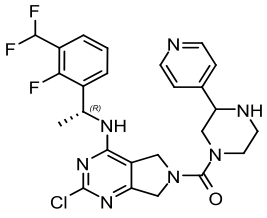
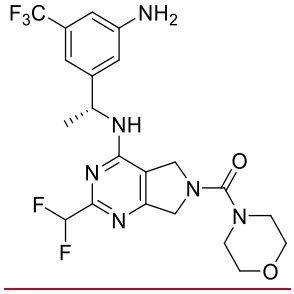
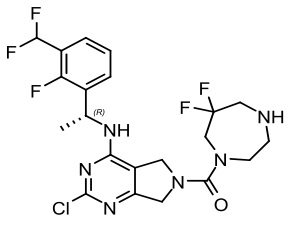
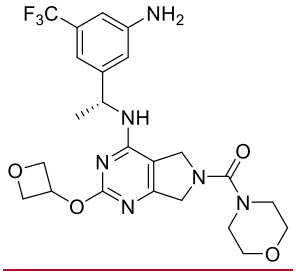
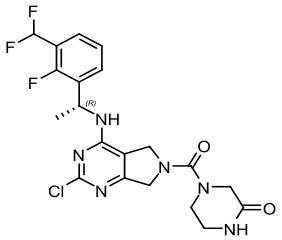
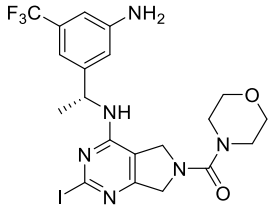
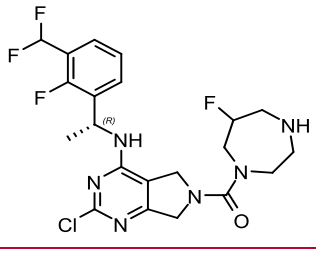
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Example 114.		Example 384.	
Example 115.		Example 385.	
Example 116.		Example 386.	

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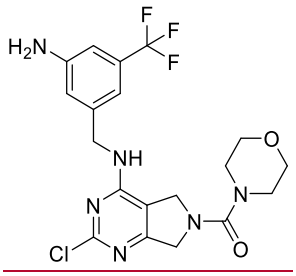
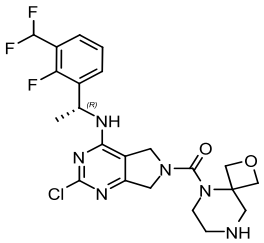
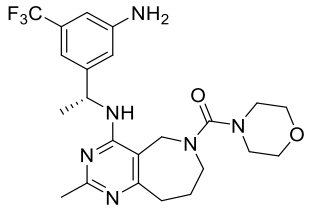
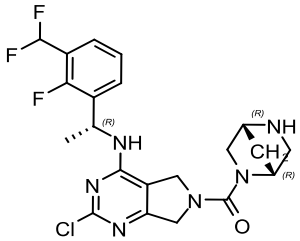
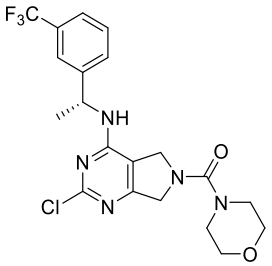
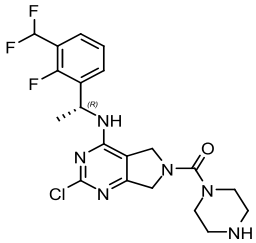
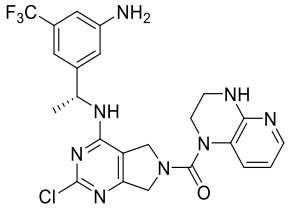
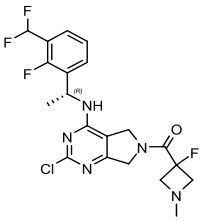
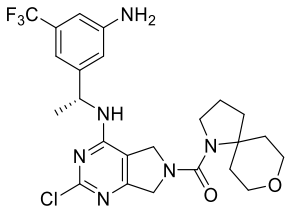
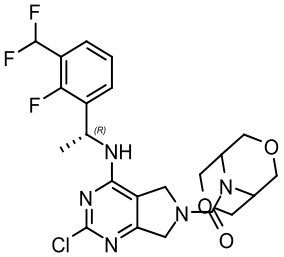
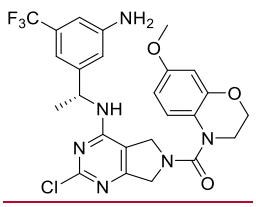
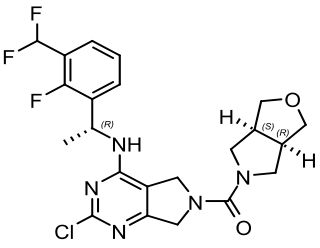
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Example 120.		Example 390.	
Example 121.		Example 391.	
Example 122.		Example 392.	

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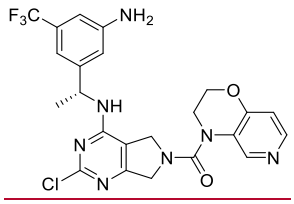
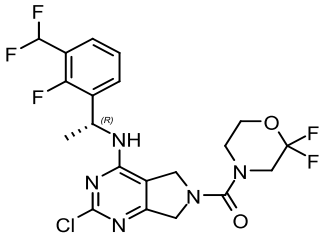
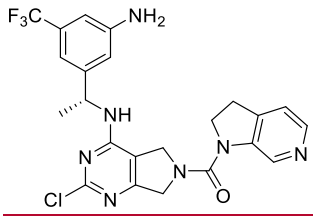
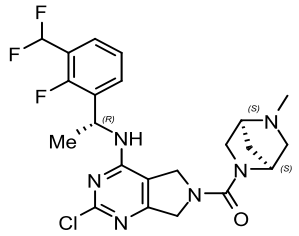
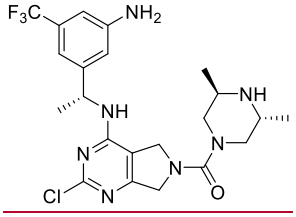
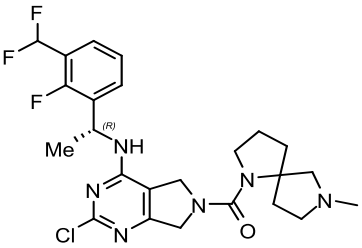
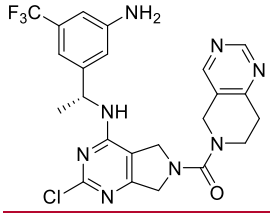
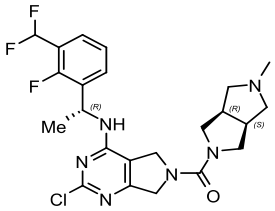
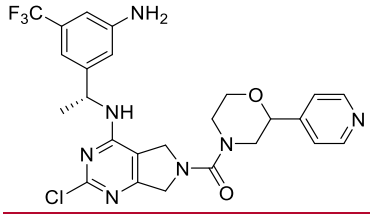
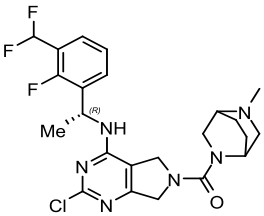
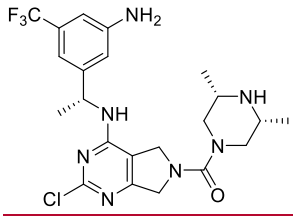
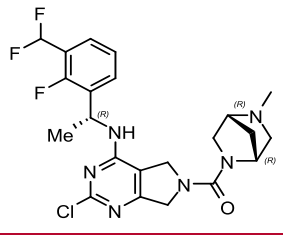
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Example 127.		Example 397.	
Example 128.		Example 398.	

Example 129.		Example 399.	
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Example 131.		Example 401.	
Example 132.		Example 402.	
Example 133.		Example 403.	
Example 134.		Example 404.	

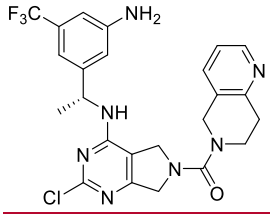
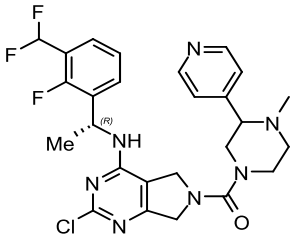
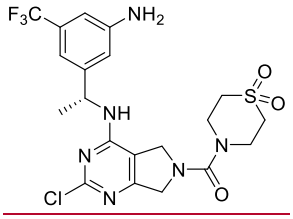
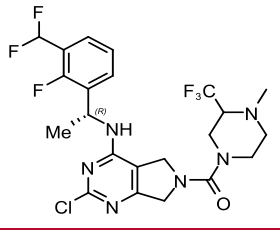
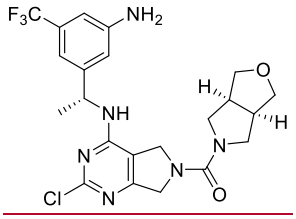
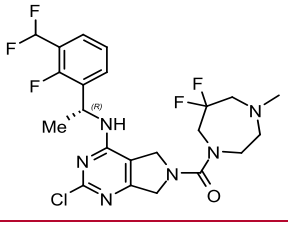
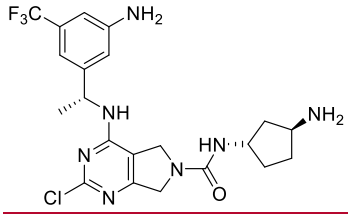
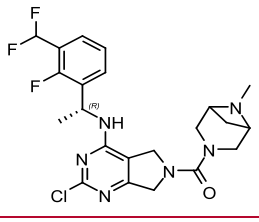
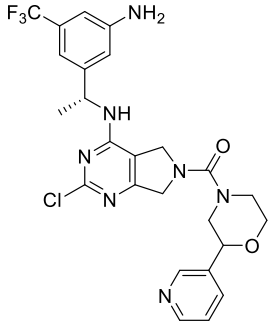
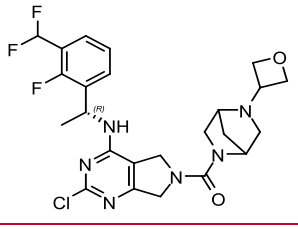
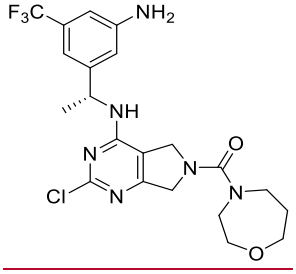
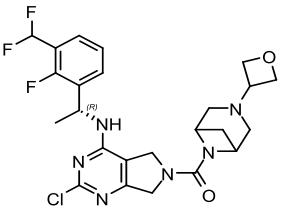
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Example 135.		Example 405.	
Example 136.		Example 406.	
Example 137.		Example 407.	
Example 138.		Example 408.	
Example 139.		Example 409.	
Example 140.		Example 410.	

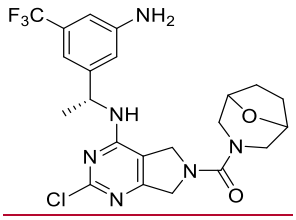
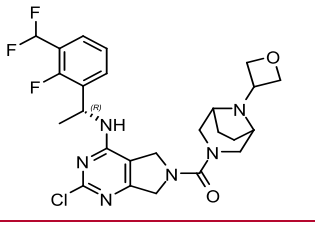
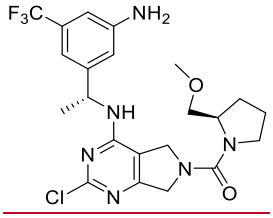
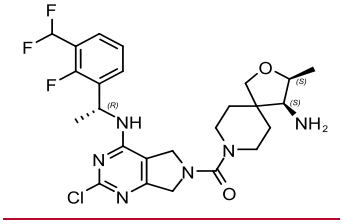
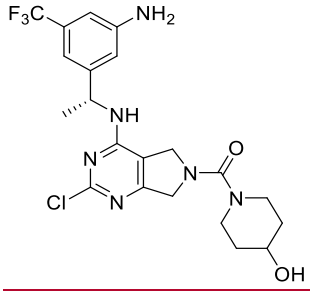
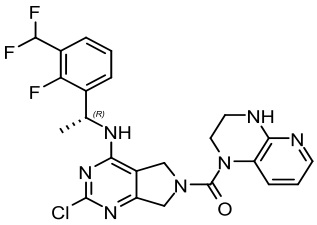
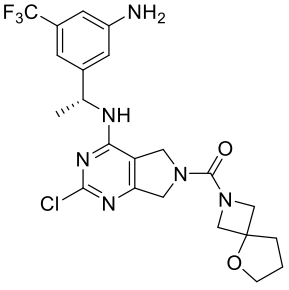
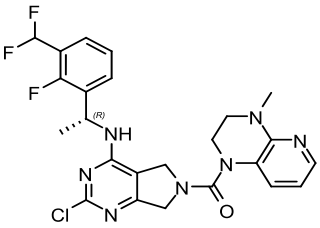
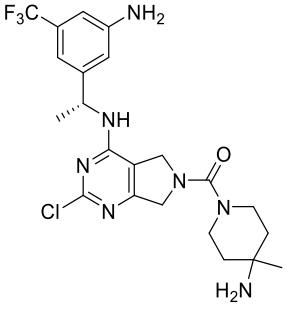
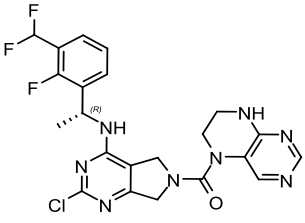
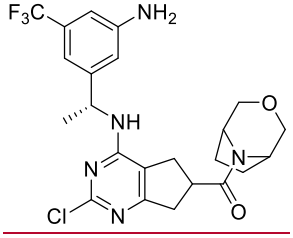
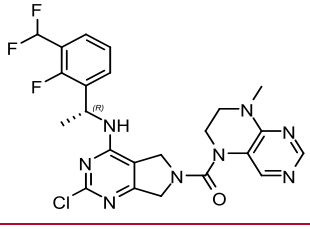
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Example 141.		Example 411.	
Example 142.		Example 412.	
Example 143.		Example 413.	
Example 144.		Example 414.	
Example 145.		Example 415.	
Example 146.		Example 416.	

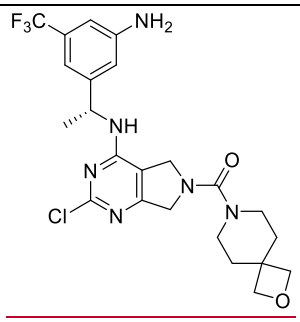
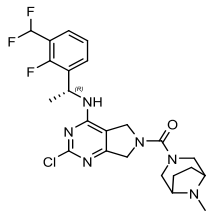
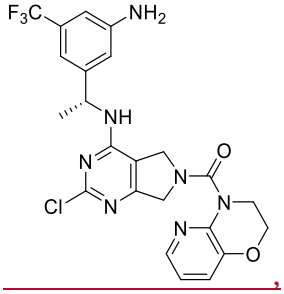
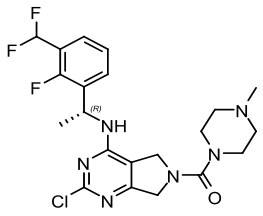
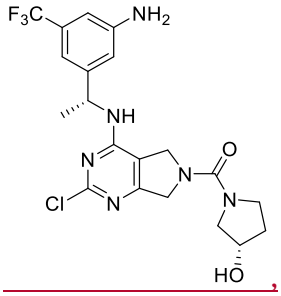
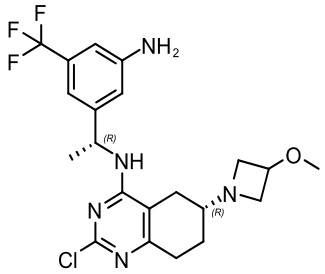
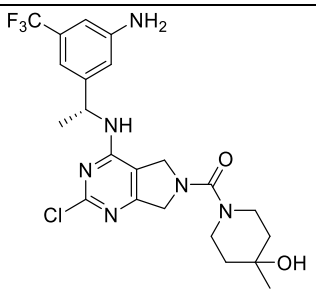
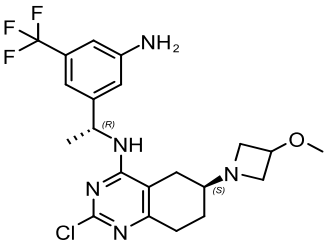
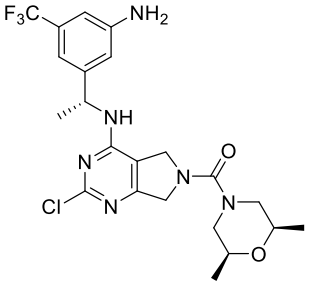
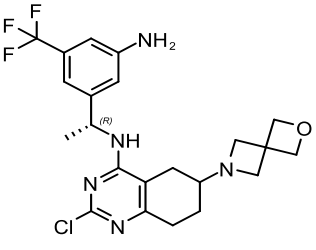
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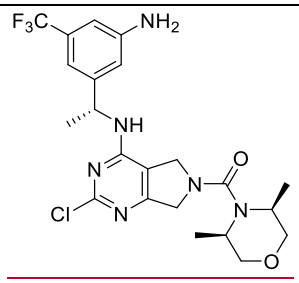
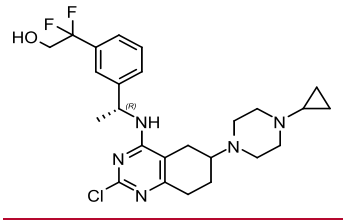
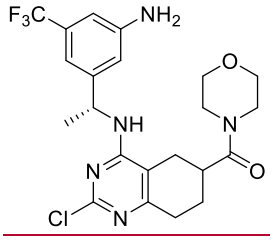
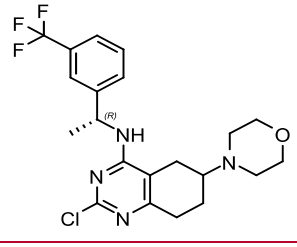
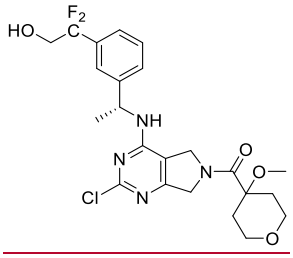
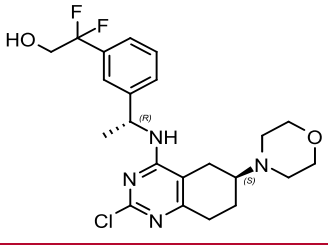
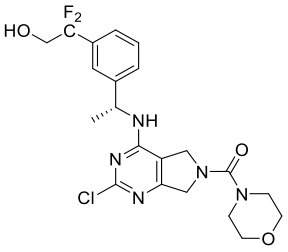
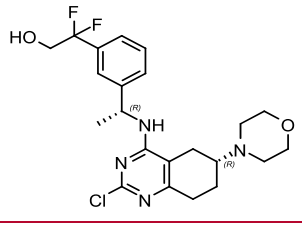
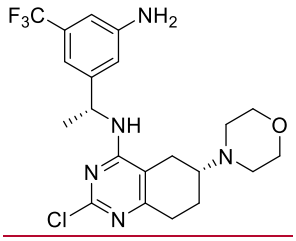
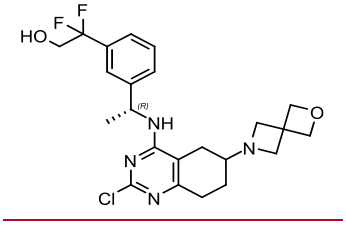
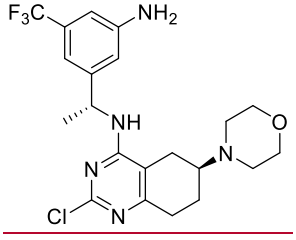
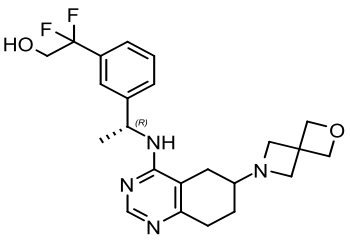
Example 147.		Example 417.	
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Example 149.		Example 419.	
Example 150.		Example 420.	
Example 151.		Example 421.	
Example 152.		Example 422.	

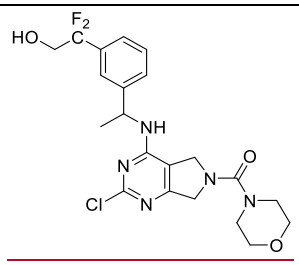
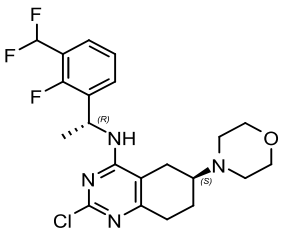
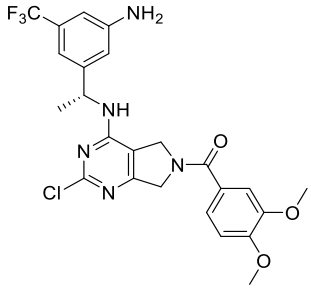
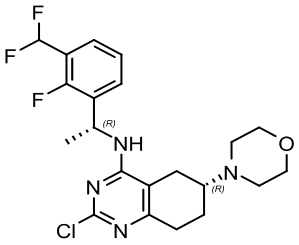
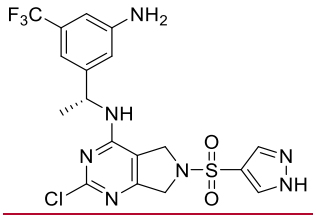
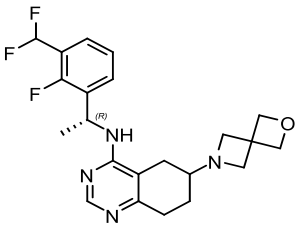
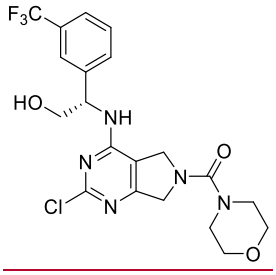
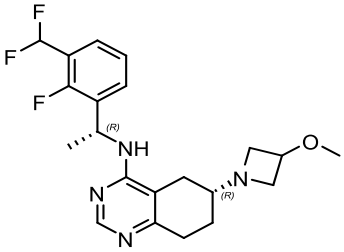
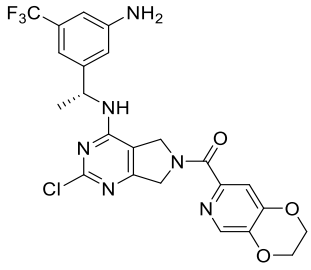
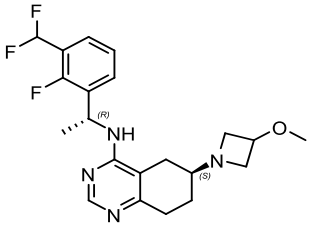
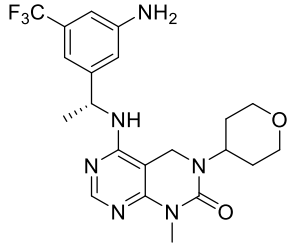
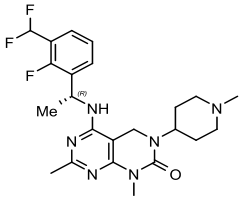
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Example 153.		Example 423.	
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Example 156.		Example 426.	
Example 157.		Example 427.	
Example 158.		Example 428.	

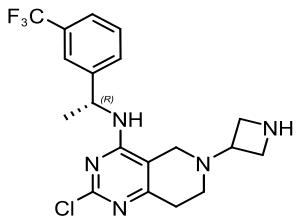
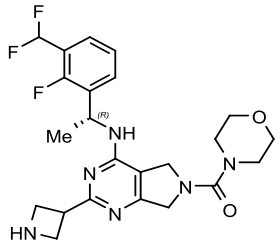
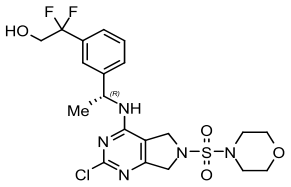
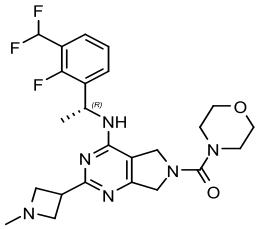
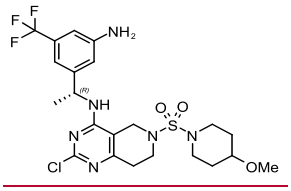
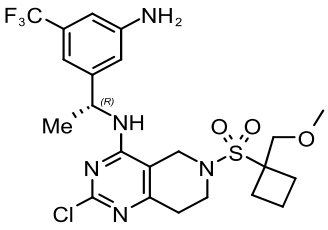
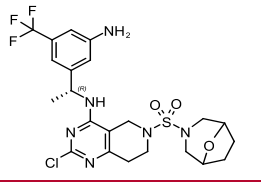
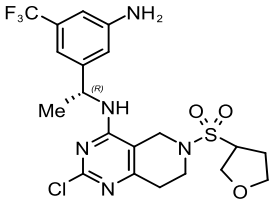
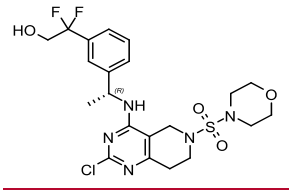
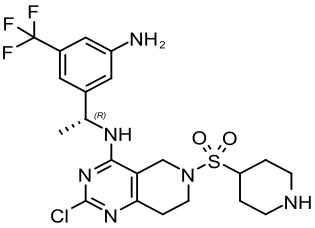
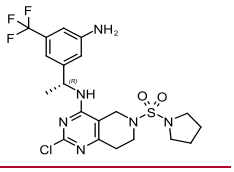
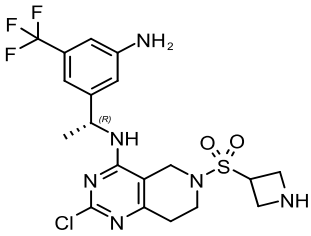
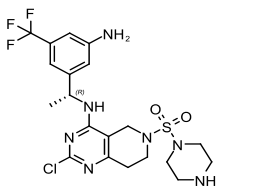
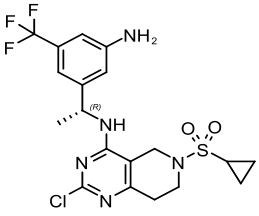
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Example 159.		Example 429.	
Example 160.		Example 430.	
Example 161.		Example 431.	
Example 162.		Example 432.	
Example 163.		Example 433.	

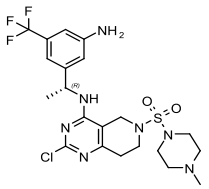
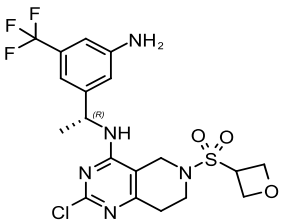
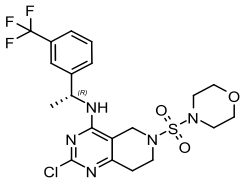
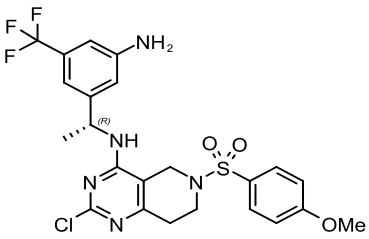
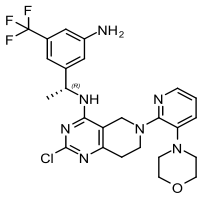
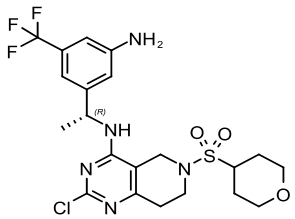
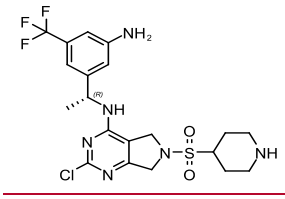
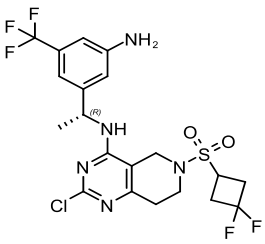
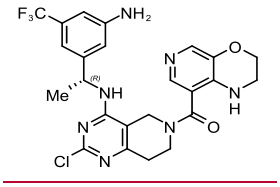
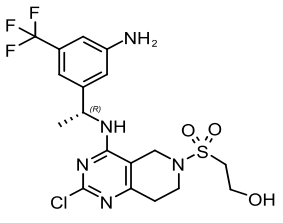
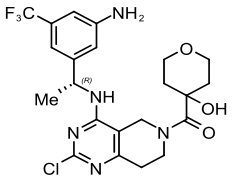
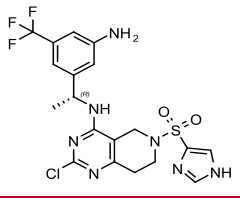
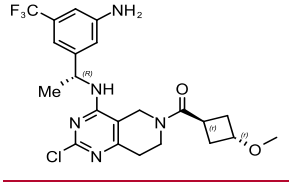
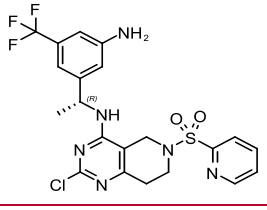
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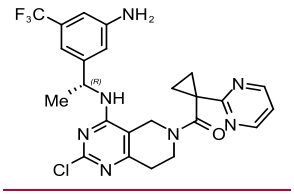
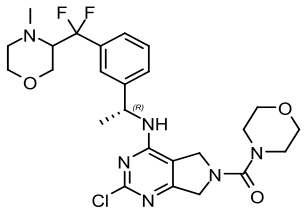
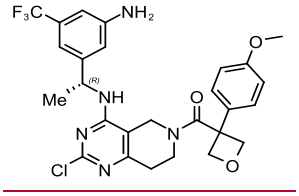
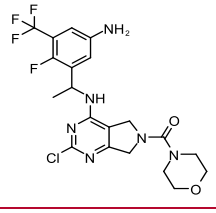
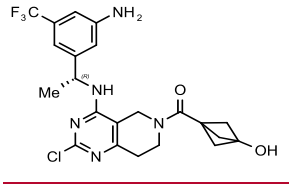
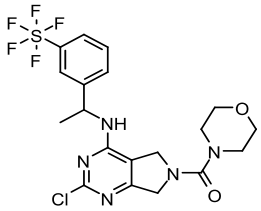
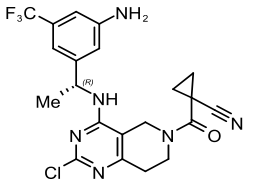
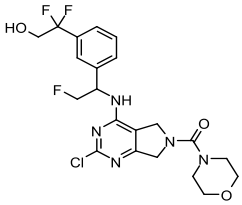
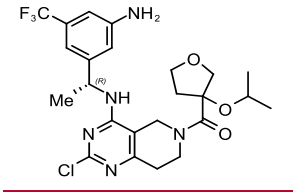
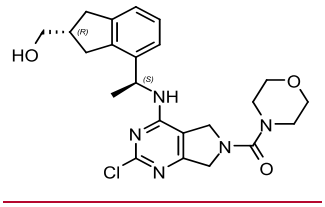
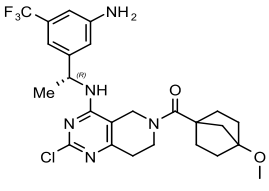
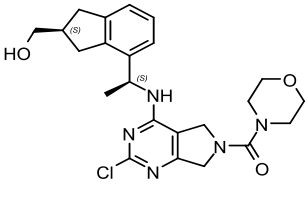
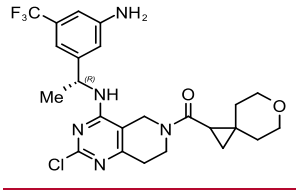
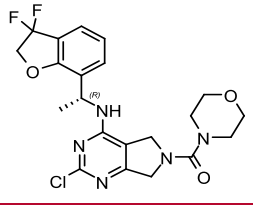
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Example 174.		Example 443.	
Example 175.		Example 444.	
Example 176.		Example 445.	

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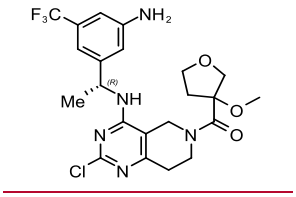
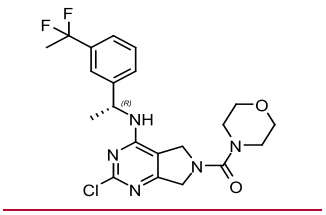
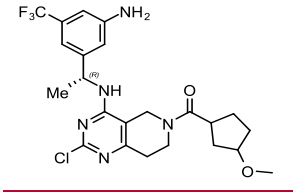
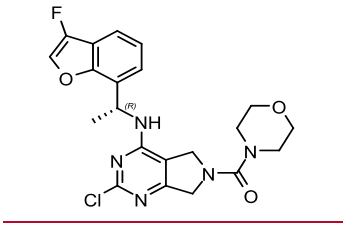
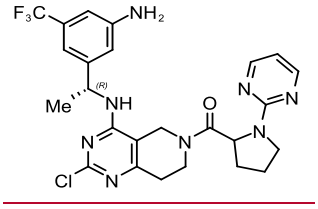
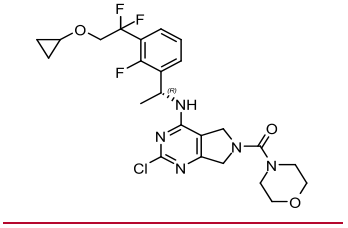
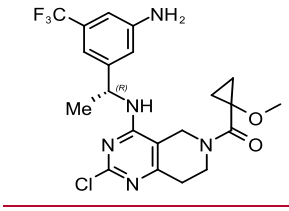
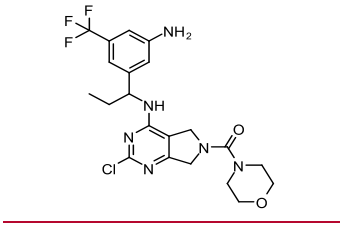
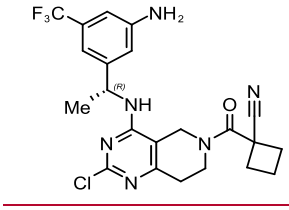
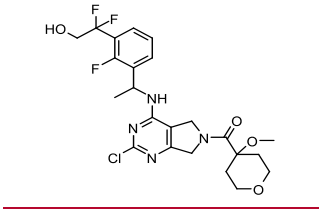
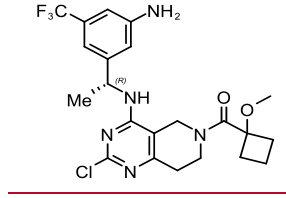
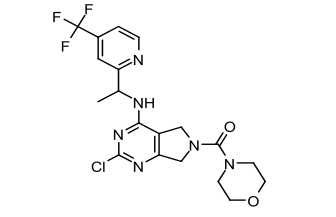
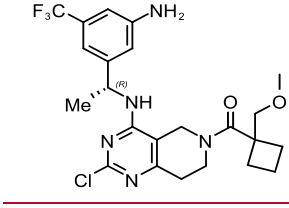
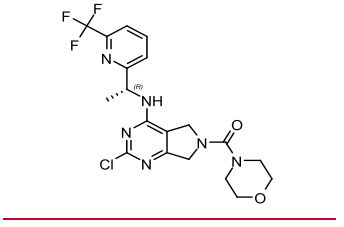
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Example 181.		Example 450.	
Example 182.		Example 451.	
Example 183.		Example 452.	

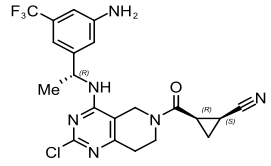
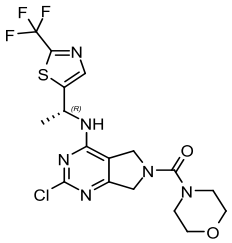
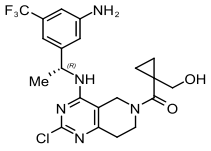
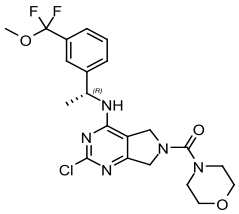
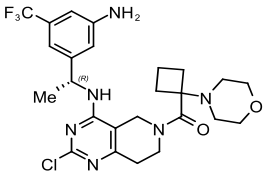
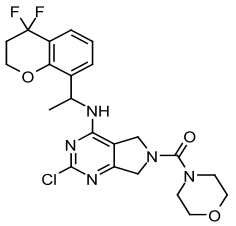
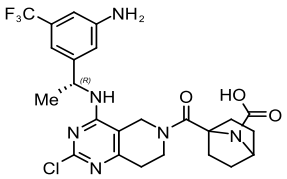
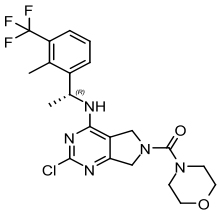
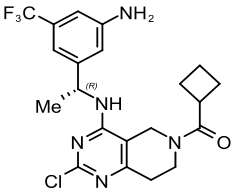
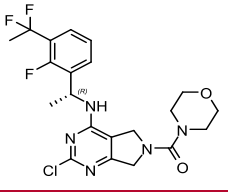
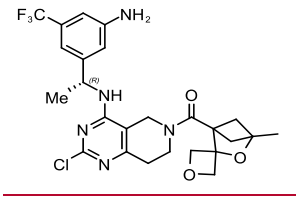
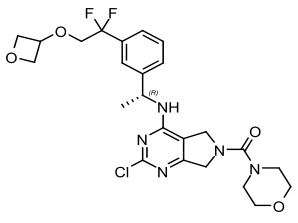
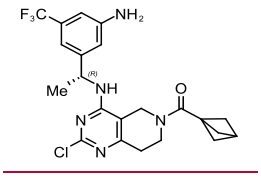
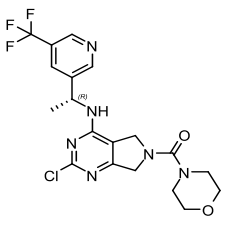
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Example 184.		Example 453.	
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Example 189.		Example 458.	
Example 190.		Example 459.	

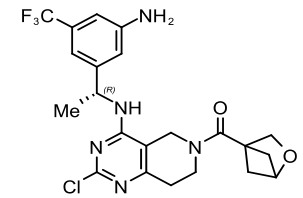
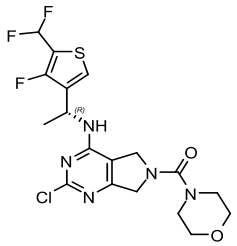
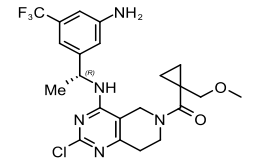
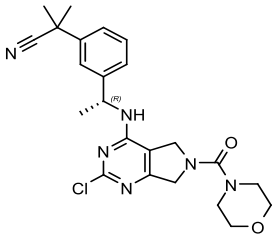
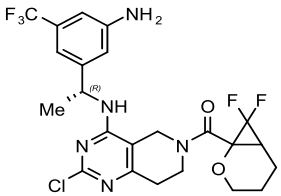
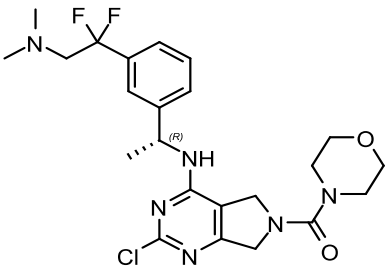
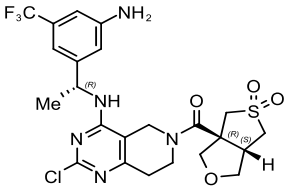
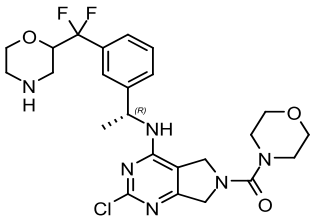
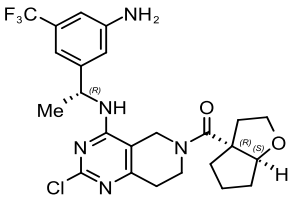
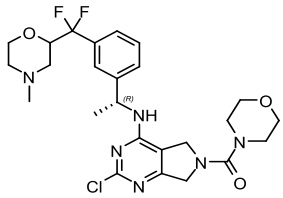
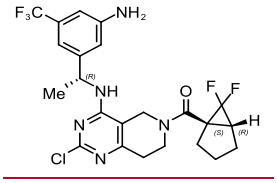
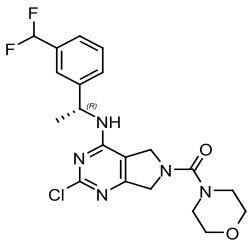
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Example 196.		Example 465.	
Example 197.		Example 466.	

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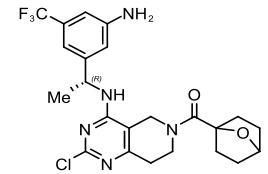
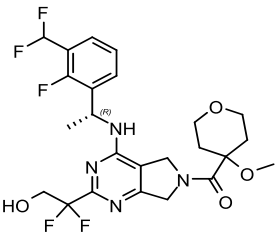
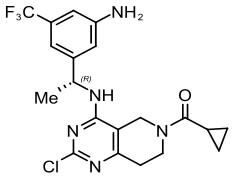
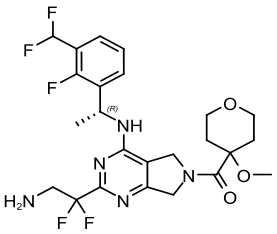
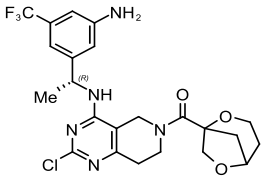
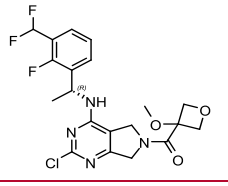
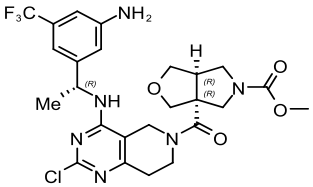
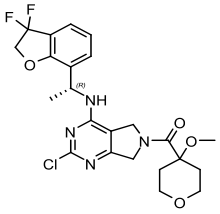
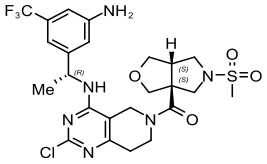
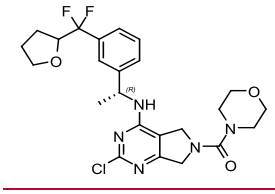
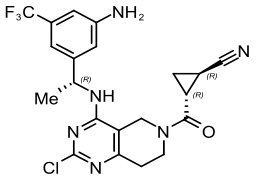
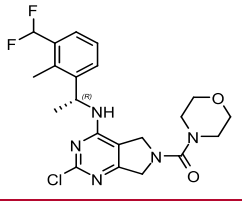
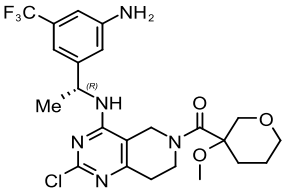
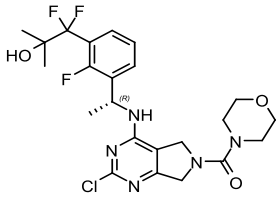
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Example 203.		Example 472.	
Example 204.		Example 473.	

Example 205.		Example 474.	
Example 206.		Example 475.	
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Example 208.		Example 477.	
Example 209.		Example 478.	
Example 210.		Example 479.	
Example 211.		Example 480.	

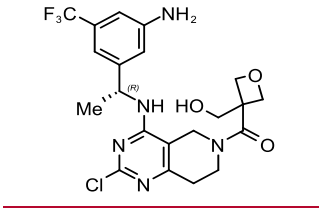
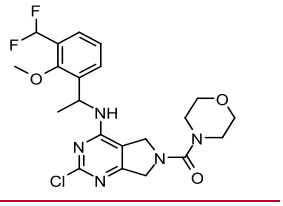
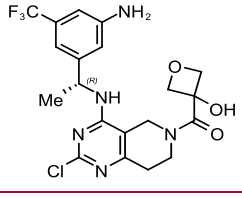
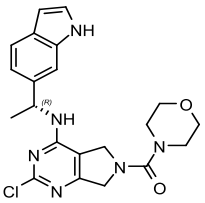
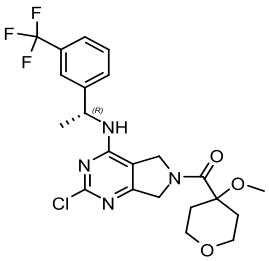
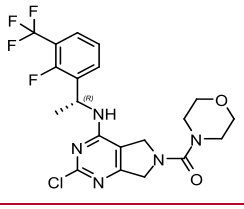
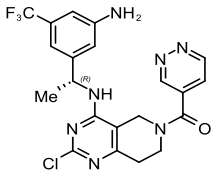
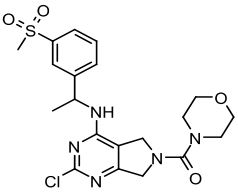
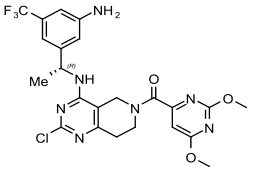
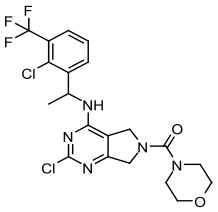
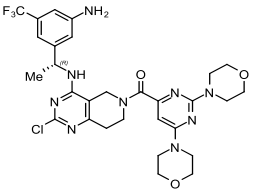
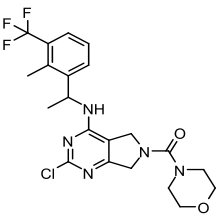
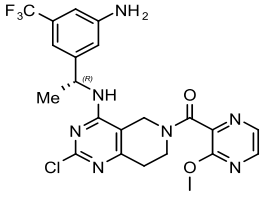
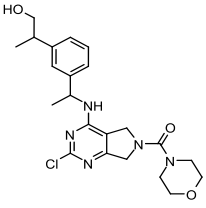
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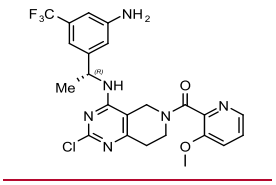
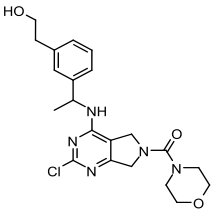
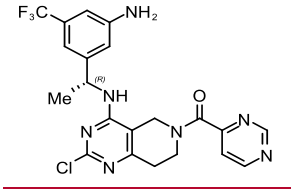
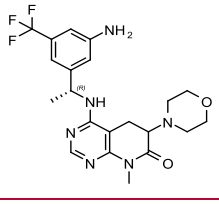
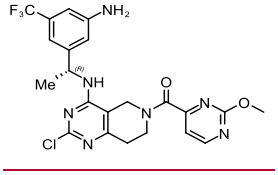
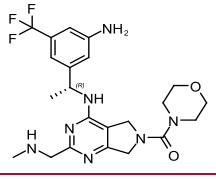
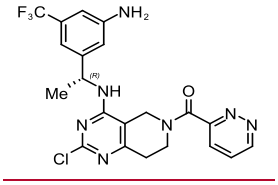
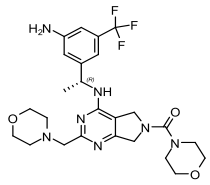
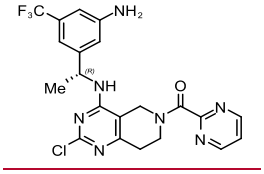
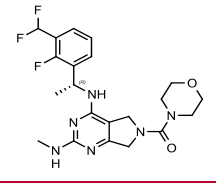
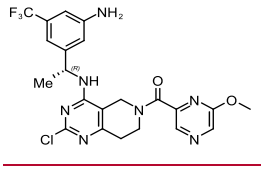
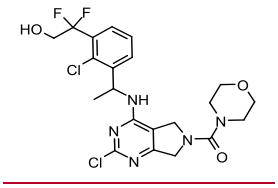
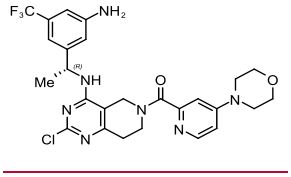
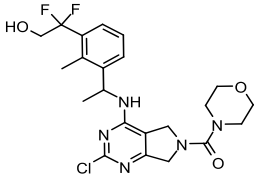
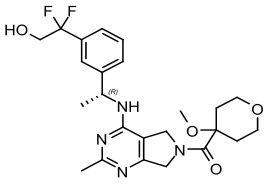
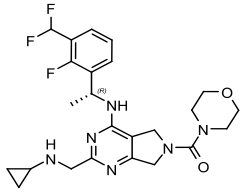
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Example 216.		Example 485.	
Example 217.		Example 486.	

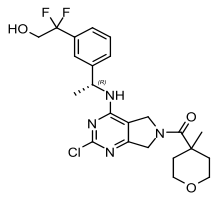
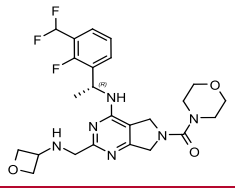
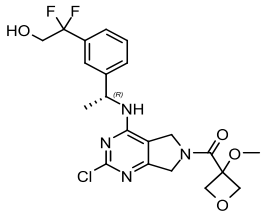
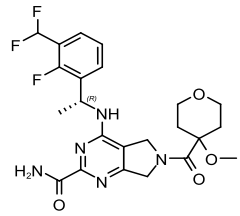
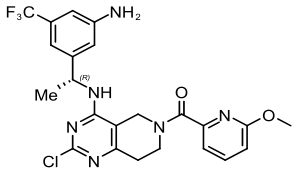
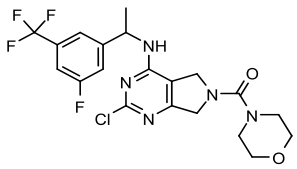
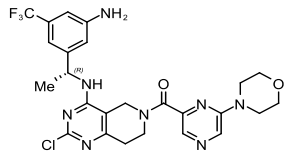
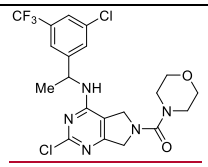
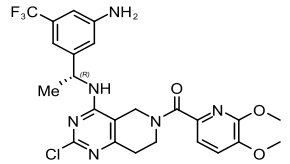
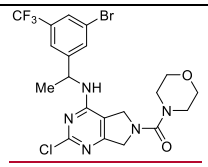
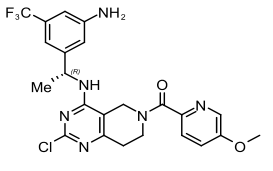
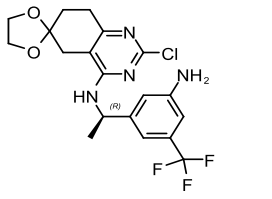
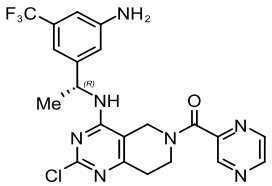
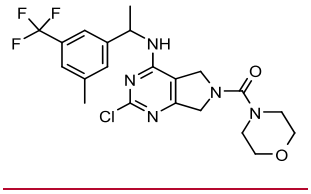
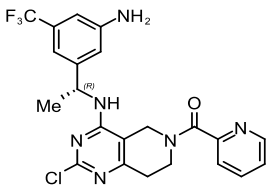
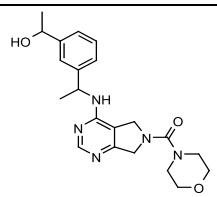
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Example 218.		Example 487.	
Example 219.		Example 488.	
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Example 221.		Example 490.	
Example 222.		Example 491.	
Example 223.		Example 492.	
Example 224.		Example 493.	

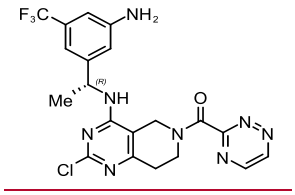
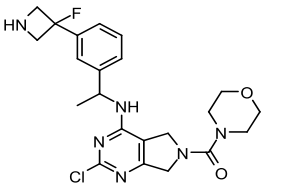
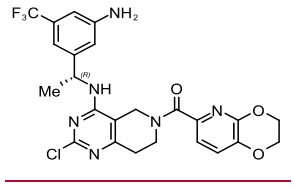
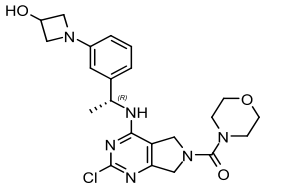
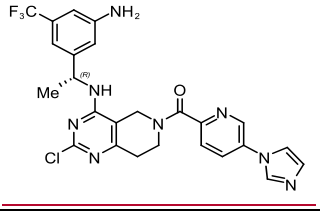
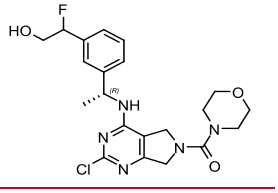
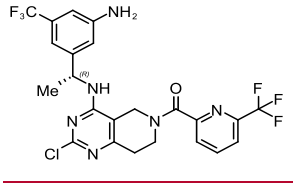
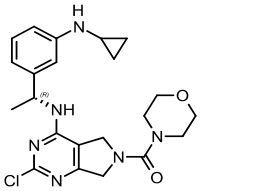
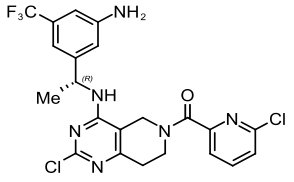
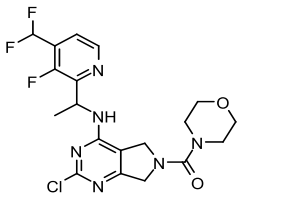
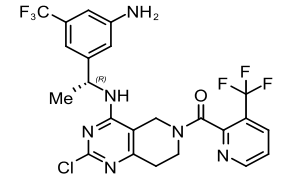
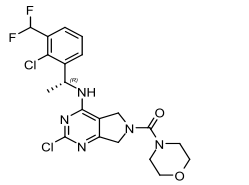
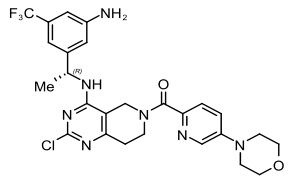
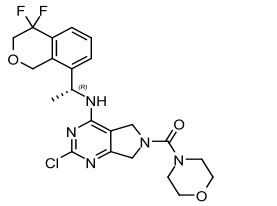
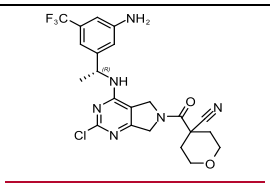
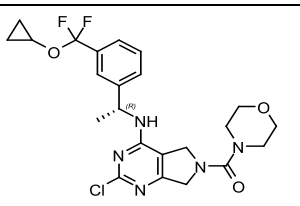
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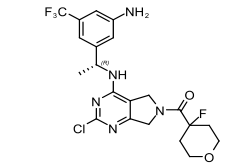
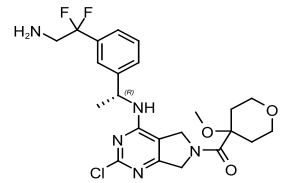
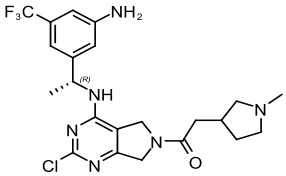
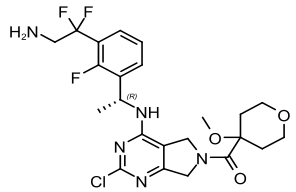
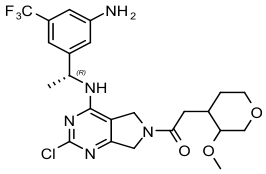
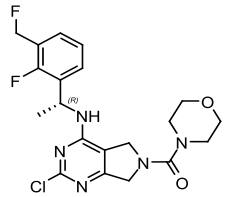
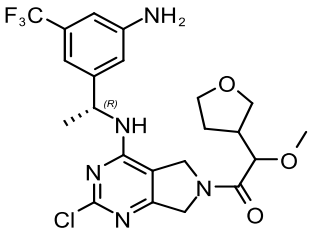
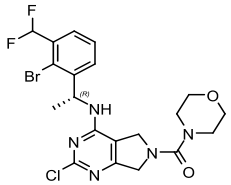
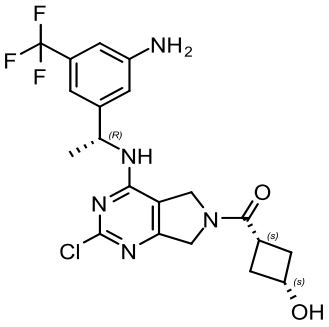
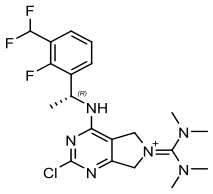
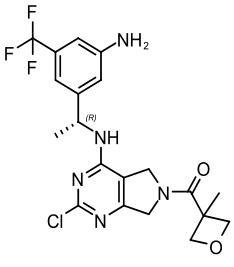
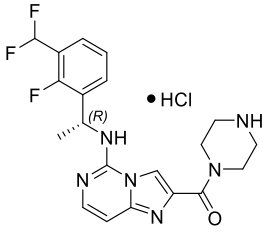
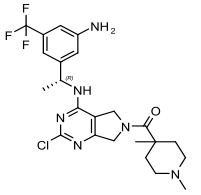
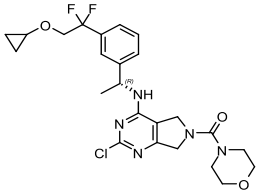
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Example 229.		Example 498.	
Example 230.		Example 499.	
Example 231.		Example 500.	

Example 232.		Example 501.	
Example 233.		Example 502.	
Example 234.		Example 503.	
Example 235.		Example 504.	
Example 236.		Example 505.	
Example 237.		Example 506.	
Example 238.		Example 507.	
Example 239.		Example 508.	

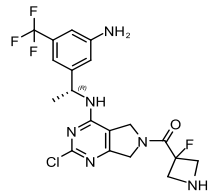
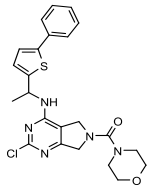
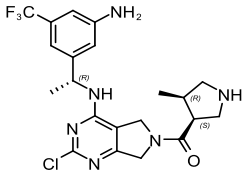
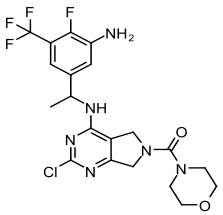
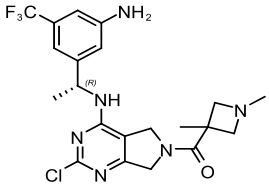
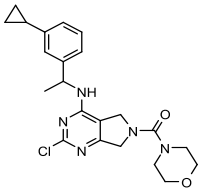
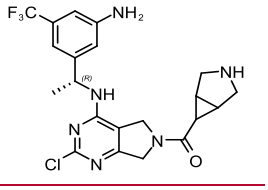
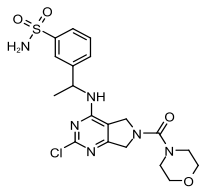
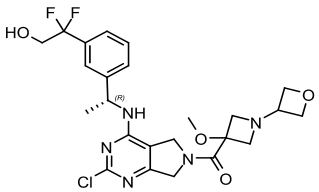
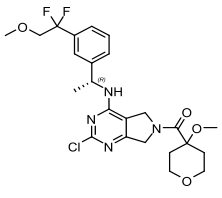
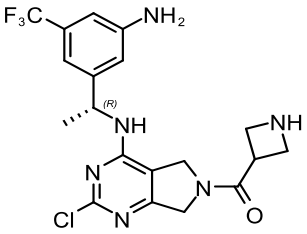
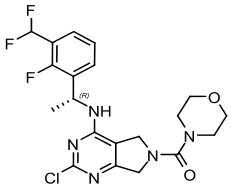
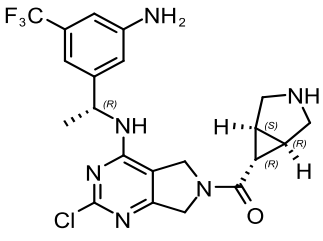
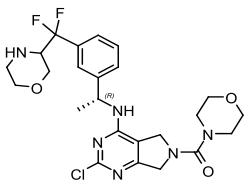
Example 240.		Example 509.	
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Example 242.		Example 511.	
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Example 244.		Example 513.	
Example 245.		Example 514.	
Example 246.		Example 515.	
Example 247.		Example 516.	

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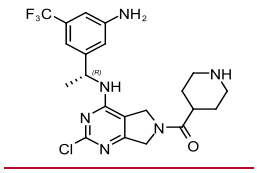
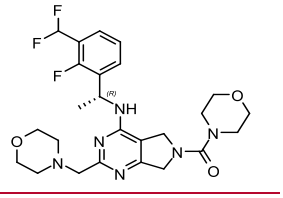
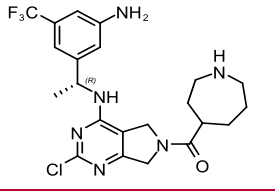
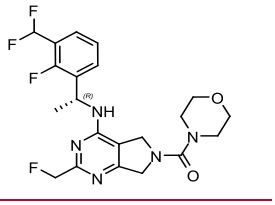
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Example 250.		Example 519.	
Example 251.		Example 520.	
Example 252.		Example 521.	
Example 253.		Example 522.	
Example 254.		Example 523.	
Example 255.		Example 524.	

Example 256.		Example 525.	
Example 257.		Example 526.	
Example 258.		Example 527.	
Example 259.		Example 528.	
Example 260.		Example 529.	
Example 261.		Example 530.	
Example 262.		Example 531.	

4at

Example 263.		Example 532.	
Example 264.		Example 533.	
Example 265.		Example 534.	
Example 266.		Example 535.	
Example 267.		Example 536.	
Example 268.		Example 537.	
Example 269.		Example 538.	

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Example 270.		**Example 539.**	
Example 271.		**Example 540.**	

[0011d] In another 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.

~~**[0011c]** 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 SOS1 in a subject.~~

~~**[0011d]** In another aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, hydate, 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.~~

~~**[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 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.~~

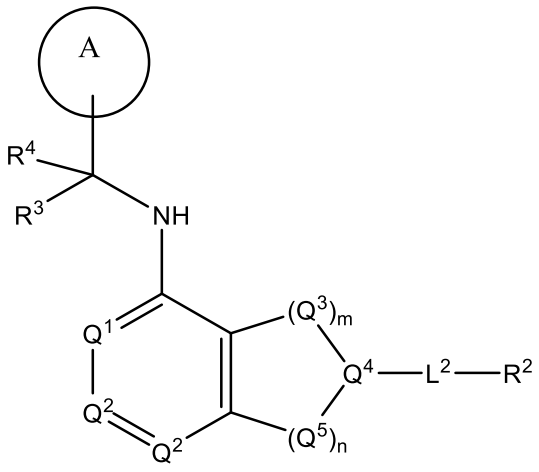
[~~0011f~~0011e] In ~~another~~ a further aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, ~~hydrate,~~

stereoisomer, or tautomer~~, or isomer~~ thereof, in the manufacture of a medicament for treating or preventing cancer in a subject in need thereof.

[~~0011g~~0011f] In ~~a further~~another 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.

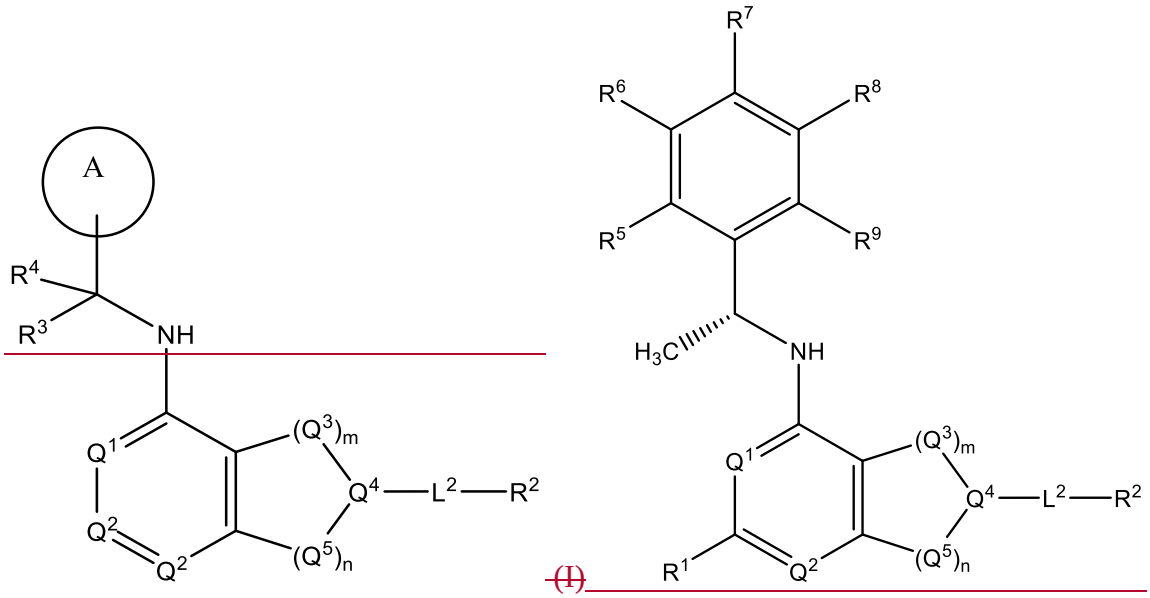
[0013] One example of the present disclosure relates to compounds of Formula (I):



(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 is ~~CH or~~ N;

Q2 is N;

Q^4 is ~~CH, C, or~~ N;

~~each Q^2 is independently C-R^1 or N, wherein one Q^2 is N and the other Q^2 is C-R^1;~~

each Q^3 and Q^5 are independently $C(R^{QC})_2$, NR^{QN}, ~~CO,~~ O, S, or SO_2, wherein each R^{QC} is independently H, F, Cl, Br, or 6-10 membered aryl, and wherein each R^{QN} is independently H, C_{1-6} alkyl, or 6-10 membered aryl;

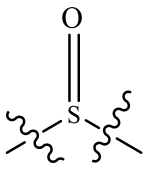
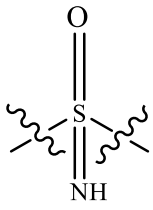
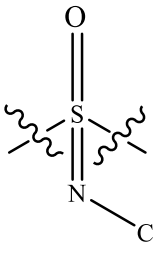
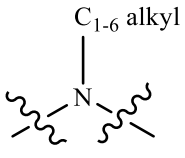
~~wherein at least one of Q^1, Q^2, Q^3, Q^4, and Q^5 is N, NR^{QN}, O, or SO_2;~~

m is 0, 1, 2, or 3;

n is 0, 1, 2, or 3;

wherein when m is 0, then n is not 0;

R^1 is selected from the group consisting of H, C_{1-6} alkyl, halogen, -$CONHR^{1a}$, -NHR^{1a}, –OR^{1a}, cyclopropyl, azetidinyl, and –CN; wherein each C_{1-6} alkyl and azetidinyl is optionally substituted with halogen, R^{1a}, -NHR^{1a}, or –OR^{1a}; wherein R^{1a} is H, C_{1-6} alkyl, cyclopropyl, 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, -$NR^{2b}R^{2c}$, -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, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} methoxyalkyl, –OH, –OR^{2a}, oxo, =N, halogen, –$C(O)R^{2a}$, –$C(O)OR^{2a}$, –$C(O)NR^{2b}R^{2c}$, -SO_2R^{2a}, –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;

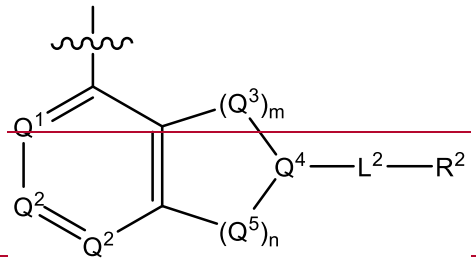
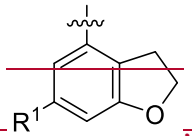
~~R^3 and R^4 are independently H or C_{1-6} alkyl optionally substituted with halo or -OH; wherein at least one of R^3 and R^4 is H or wherein R^3 and R^4 together with the atom to which they are attached combine to form a 3-6 membered cycloalkyl; and~~

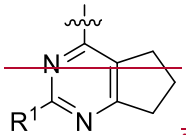
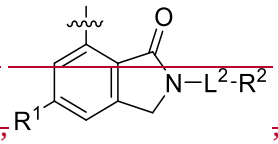
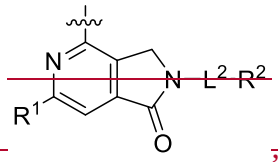
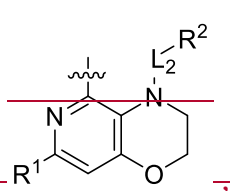
~~A is an optionally substituted 6-membered aryl or an optionally substituted 5-6 membered heteroaryl;~~

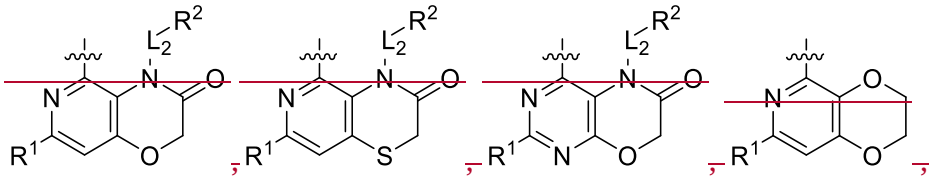
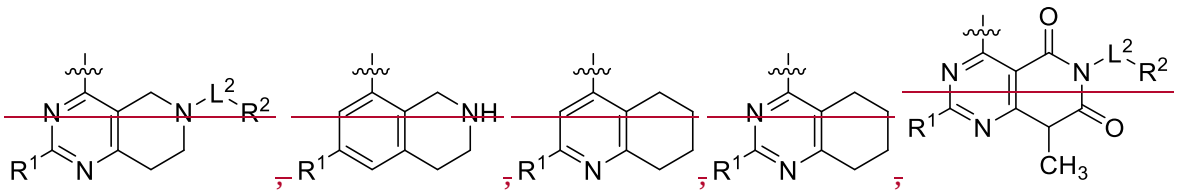
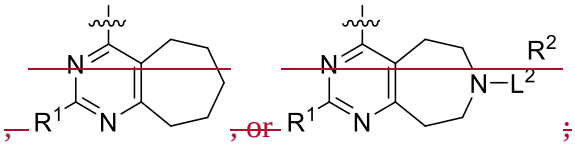
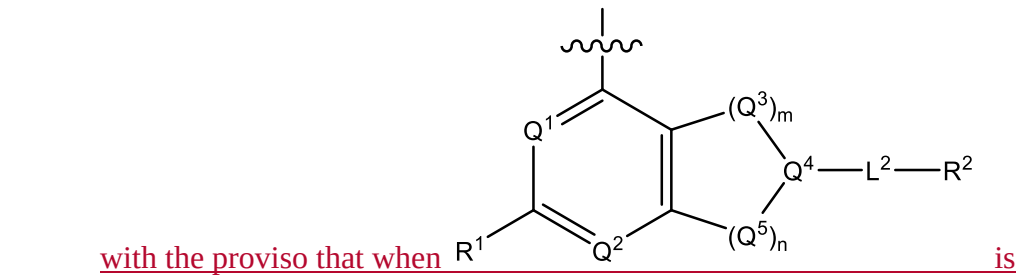
R^5, R^6, R^7, R^8, and R^9 are independently selected from the group consisting of H, D, C_{1-6} alkyl, C_{2-6} alkenyl, 4-8 membered cycloalkenyl, C_{2-6} alkynyl, 3-8 membered cycloalkyl, 3-14 membered heterocyclyl, -OH, halogen, $–NO_2$, –CN, $–NR^{11}R^{12}$, $–SR^{10}$, $–S(O)_2NR^{11}R^{12}$, $–S(O)_2R^{10}$, $–NR^{10}S(O)_2NR^{11}R^{12}$, $–NR^{10}S(O)_2R^{11}$, $–S(O)NR^{11}R^{12}$, $–S(O)R^{10}$, $–NR^{10}S(O)NR^{11}R^{12}$, $–NR^{10}S(O)R^{11}$, $–C(O)R^{10}$, and $–CO_2R^{10}$, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, 4-8 membered cycloalkenyl, C_{2-6} alkynyl, 3-8 membered cycloalkyl, and 3-14 membered heterocyclyl are independently optionally substituted with –OH, halogen, $–NO_2$, oxo, –CN, $–R^{10}$, $–OR^{10}$, $–NR^{11}R^{12}$, $–SR^{10}$, $–S(O)_2NR^{11}R^{12}$, $–S(O)_2R^{10}$, $–NR^{10}S(O)_2NR^{11}R^{12}$, $–NR^{10}S(O)_2R^{11}$, $–S(O)NR^{11}R^{12}$, $–S(O)R^{10}$, $–NR^{10}S(O)NR^{11}R^{12}$, $–NR^{10}S(O)R^{11}$, 3-8 membered cycloalkyl, 3-14 membered heterocyclyl, 6-10 membered aryl, or 5-10 membered heteroaryl, or any two adjacent R^5, R^6, R^7, R^8, and R^9 form a 3-14 membered fused ring;

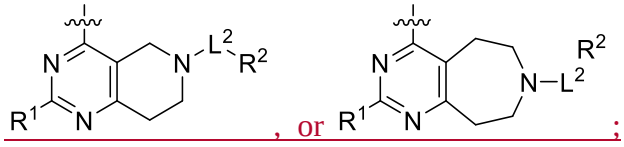
R^{10}, R^{11}, and R^{12} are at each occurrence independently selected from H, D, C_{1-6} alkyl, C_{2-6} alkenyl, 4-8 membered cycloalkenyl, C_{2-6} alkynyl, 3-8 membered cycloalkyl, 3-14 membered heterocyclyl, $–OR^{13}$, $–SR^{13}$, halogen, $–NR^{13}R^{14}$, $–NO_2$, and –CN; and

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;

~~with the proviso that when~~  ~~is~~ ,

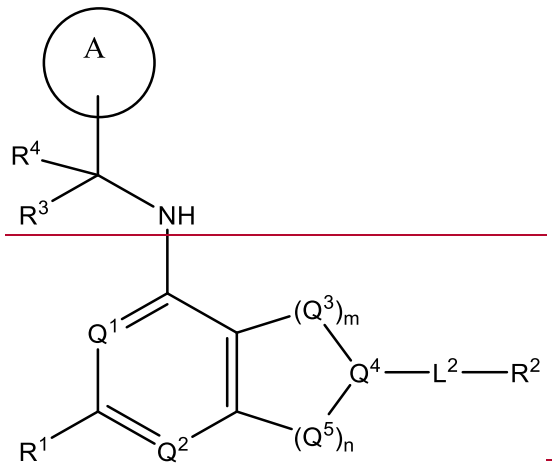
, , , , ,

with the proviso that when  is , or ;

then R^1 is not H.

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



~~(I-a)~~

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

~~Q^1, Q^3, Q^4, Q^5, m, n and A are as defined in claim 1;~~

~~Q^2 is CH or N;~~

~~wherein at least one of Q^1, Q^2, Q^3, Q^4, and Q^5 is N, NR^{QN}, O, or SO_2;~~

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–, $–C(O)NH(CH_2)_o–$, $–S(O)_2–$, $–C(O)(CH_2)_p–$, $–(CH_2)_p–$, or –O–; wherein o is 0, 1, or 2; and wherein p is a number from 1 to 6; and

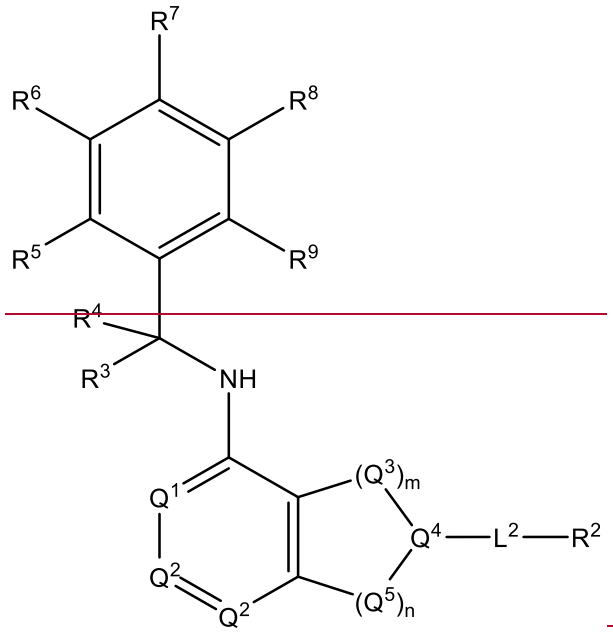
R^2 is selected from the group consisting of H, $–(CH_2)_qCH_3$, 3-14 membered cycloalkyl, 3-14 membered cycloalkenyl, 3-14 membered heterocyclyl, 6-10 membered aryl, and 5-10 membered heteroaryl; wherein q is a number from 1 to 5; wherein each 3-14 membered cycloalkyl, 3-14 membered cycloalkenyl, 3-14 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~~

~~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~~.

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

~~4. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, isomer, prodrug, or tautomer thereof, wherein A is an optionally substituted 5-6 membered heteroaryl.~~

5. The compound of claim 1 having the structure of Formula (V),



(V)

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

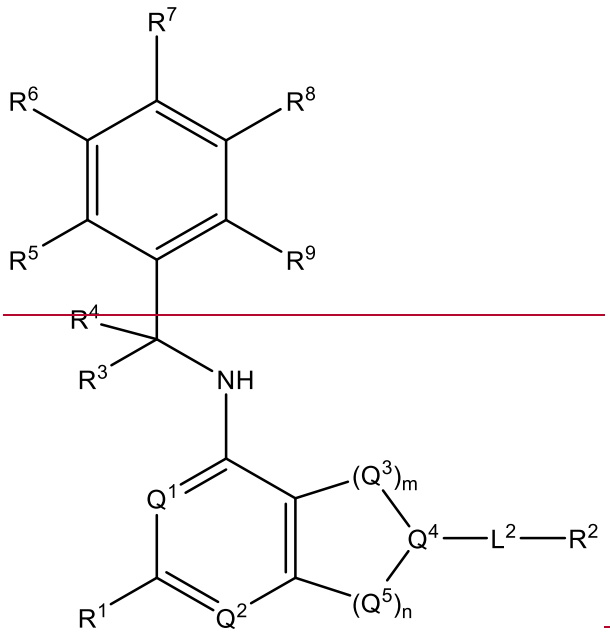
L^2, Q^1, Q^2, Q^3, Q^4, Q^5, m, n, R^1, R^2, R^3 and R^4 are as defined in claim 1;

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, 3-14 membered heterocyclyl, -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, 3-8 membered cycloalkyl, and 3-14 membered heterocyclyl are independently optionally substituted with OH, halogen, NO_2, oxo, CN, $-R^{10}$, OR^{10}, $NR^{11}R^{12}$, $-SR^{10}$, $S(O)_2NR^{11}R^{12}$, $S(O)_2R^{10}$, $NR^{10}S(O)_2NR^{11}R^{12}$, $NR^{10}S(O)_2R^{11}$, $S(O)NR^{11}R^{12}$, $S(O)R^{10}$, $NR^{10}S(O)NR^{11}R^{12}$, $NR^{10}S(O)R^{11}$, 3-8 membered cycloalkyl, 3-14 membered heterocyclyl, 6-10 membered aryl, or 5-10 membered heteroaryl, or any two adjacent R^5, R^6, R^7, R^8, and R^9 forms a 3-14 membered fused ring;

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.~~

~~6~~3. The compound of claim 1 ~~5 having the structure of Formula (V-a),~~



~~(V-a)~~

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

~~Q^1, Q^3, Q^4, Q^5, m, n, 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 5;~~

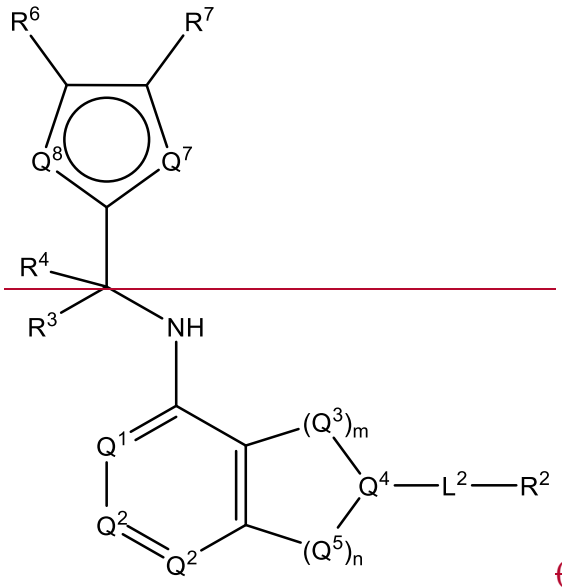
~~Q^2 is CH or N;~~

~~wherein at least one of Q^1, Q^2, Q^3, Q^4, and Q^5 is N, NR^{QN}, O, or SO_2;~~

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–, $–C(O)NH(CH_2)_o–$, $–S(O)_2–$, $–C(O)(CH_2)_p–$, $–(CH_2)_p–$, or –O–; wherein o is 0, 1, or 2; and wherein p is a number from 1 to 6.

7. The compound of claim 1 having the structure of Formula (VI),



(VI)

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

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

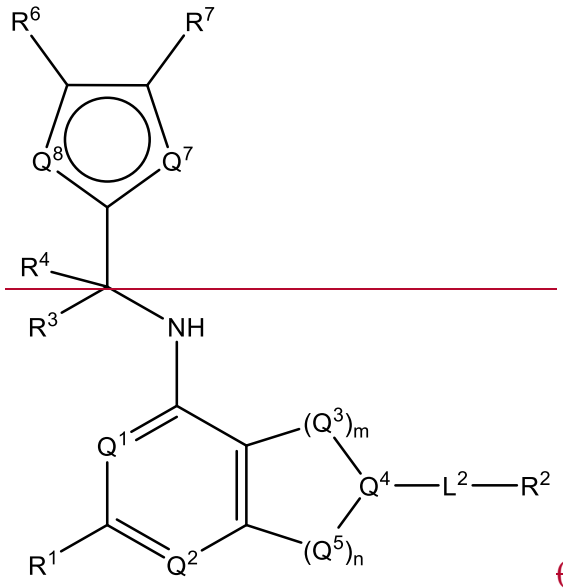
Q^7 and Q^8 are each independently CH, N, NH, O, or S, provided at least one of Q^7 and Q^8 is N, NH, O, or S;

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, 3-14 membered heterocyclyl, –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, 3-8 membered cycloalkyl, and 3-14 membered heterocyclyl are independently optionally substituted with –OH, halogen, $–NO_2$, oxo, –CN, $–R^{10}$, $–OR^{10}$, $–NR^{11}R^{12}$, $–SR^{10}$, $–S(O)_2NR^{11}R^{12}$, $–S(O)_2R^{10}$, $–NR^{10}S(O)_2NR^{11}R^{12}$, $–NR^{10}S(O)_2R^{11}$, $–S(O)NR^{11}R^{12}$, $–S(O)R^{10}$, $–NR^{10}S(O)NR^{11}R^{12}$, $–NR^{10}S(O)R^{11}$, 3-8 membered cycloalkyl, 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.~~

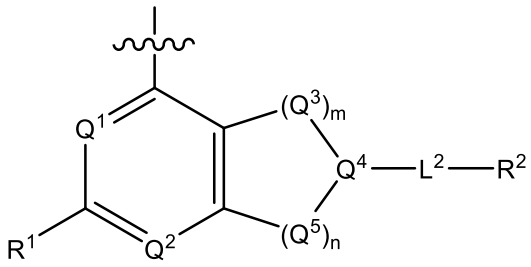
~~8. The compound of claim 7, or a pharmaceutically acceptable salt, solvate, isomer, prodrug, or tautomer thereof, having the structure (VI-a),~~



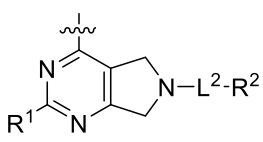
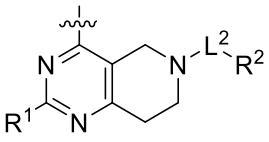
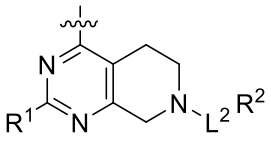
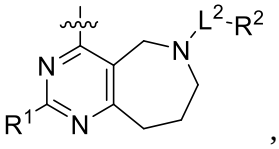
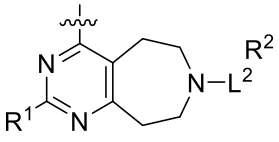
~~(VI-a)~~

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

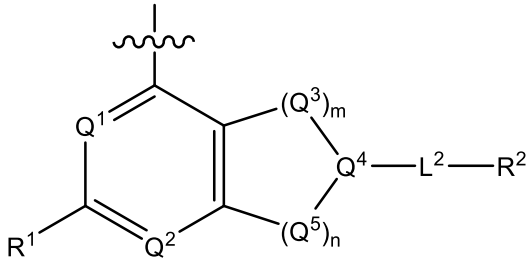
~~9~~4. The compound of claim ~~1~~2, or a pharmaceutically acceptable salt, solvate, stereoisomer, ~~isomer, prodrug,~~ or tautomer thereof, wherein

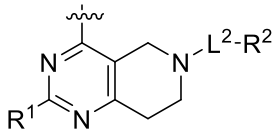
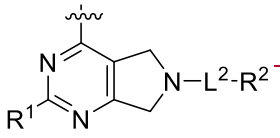


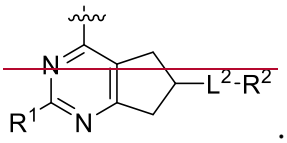
is selected from the group consisting of

, , , , and .

~~10~~5. The compound of claim ~~1~~2, or a pharmaceutically acceptable salt, solvate, stereoisomer, ~~isomer, prodrug,~~ or tautomer thereof, wherein

 is selected from the group consisting of

 and  ~~and~~

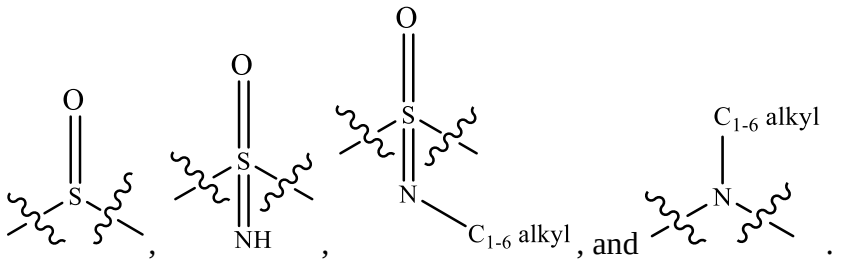
.

~~11~~6. The compound of any one of claims 1-~~10~~5, or a pharmaceutically acceptable salt, solvate, stereoisomer, ~~isomer, prodrug,~~ or tautomer thereof, wherein 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.

~~12~~7. The compound of any one of claims 1-~~10~~5, or a pharmaceutically acceptable salt, solvate, stereoisomer, ~~isomer, prodrug,~~ or tautomer thereof, wherein R^1 is H, halogen, C_{1-6} alkyl, cyclopropyl, –CN, or –OR^{1a}; wherein R^{1a} is H or C_{1-6} alkyl.

~~13~~8. The compound of any one of claims 1-~~12~~7, 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$(CH_2)_o$–, –$S(O)_2$–, –

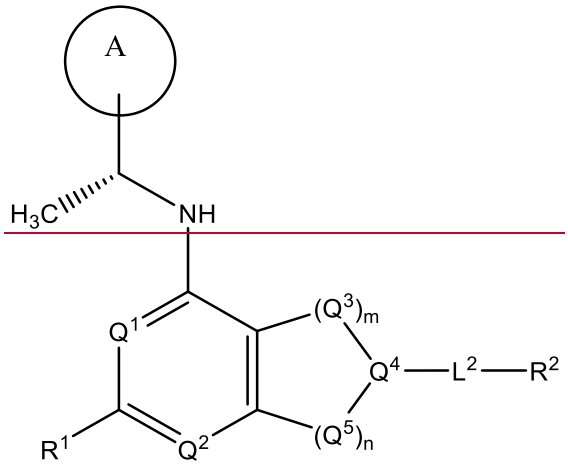
$C(O)(CH_2)_p$–, –$(CH_2)_p$–, and –O–; wherein o is 0, 1, or 2; and wherein p is a number from 1 to 6.

~~14~~9. The compound of any one of claims 1-~~12~~7, or a pharmaceutically acceptable salt, solvate, stereoisomer ~~isomer, prodrug~~, or tautomer thereof, wherein L^2 is selected from the group consisting of , and .

~~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^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, =N, 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.

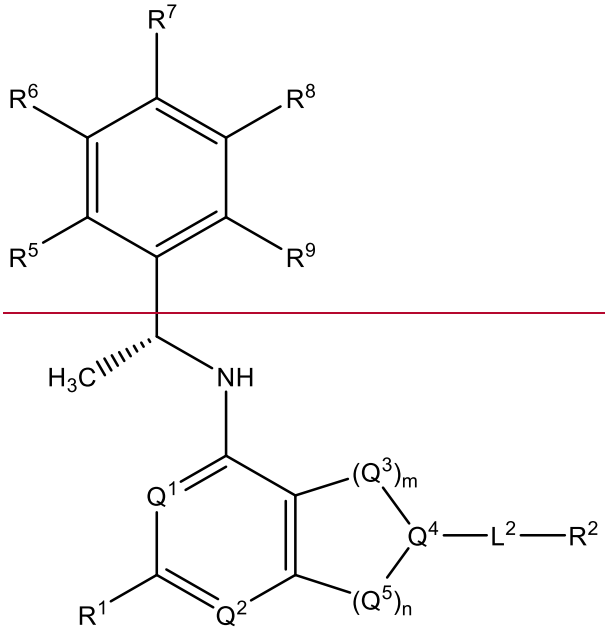
~~16~~11. The compound of any one of claims 1-~~14~~9, or a pharmaceutically acceptable salt, solvate, stereoisomer, ~~isomer, prodrug,~~ or tautomer thereof, wherein R^2 is 3-14 membered heterocyclyl, wherein the 3-14 membered heterocyclyl is optionally substituted with C_{1-6} alkyl optionally substituted with halogen or –OR^{2a}, –OH, –OR^{2a}, oxo, =N, halogen, –$C(O)R^{2a}$, –$C(O)OR^{2a}$, –$C(O)NR^{2b}R^{2c}$, -SO_2R^{2a}, –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; and wherein R^{2c} is H or C_{1-6} alkyl.

~~17. The compound of claim 2, or a pharmaceutically acceptable salt, solvate, isomer, prodrug, or tautomer thereof, wherein R^3 is H and R^4 is CH_3 and the compound is of the following formula:~~



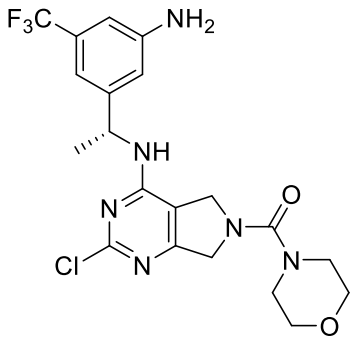
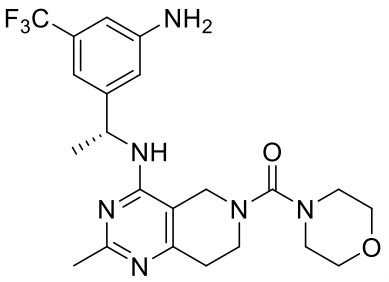
~~wherein A, L^2, Q^1, Q^2, Q^3, Q^4, Q^5, R^1, R^2, m and n are as defined in claim 2.~~

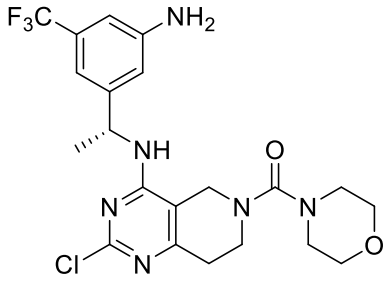
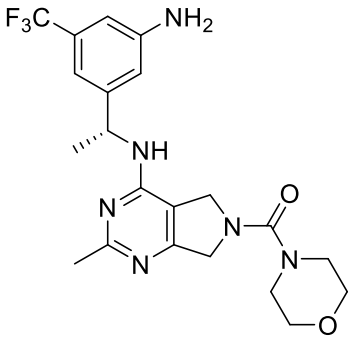
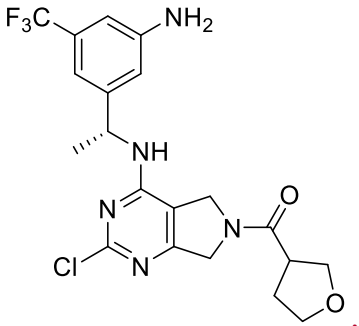
~~18. The compound of claim 5, or a pharmaceutically acceptable salt, solvate, isomer, prodrug, or tautomer thereof, wherein R^3 is H and R^4 is CH_3 and the compound is of the following formula:~~

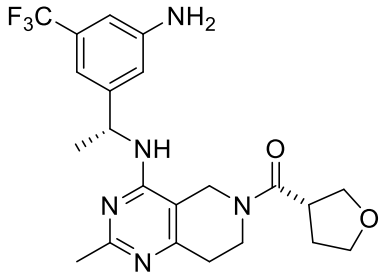
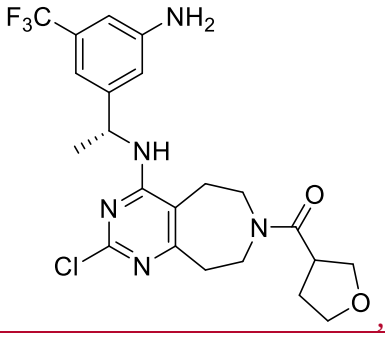


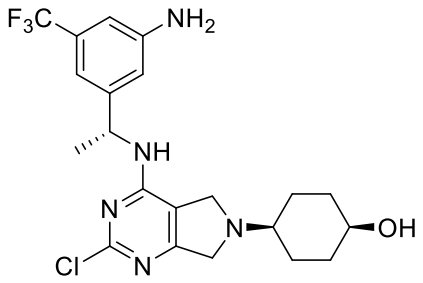
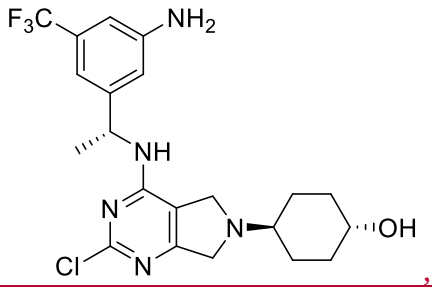
~~wherein L^2, Q^1, Q^2, Q^3, Q^4, Q^5, R^1, R^2, R^4, R^5, R^6, R^7, R^8, R^9, m and n are as defined in claim 5.~~

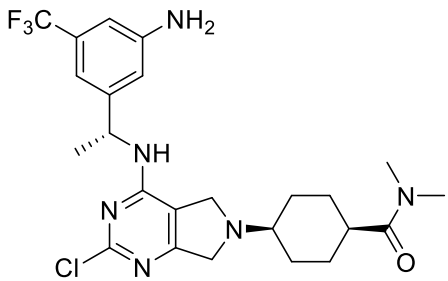
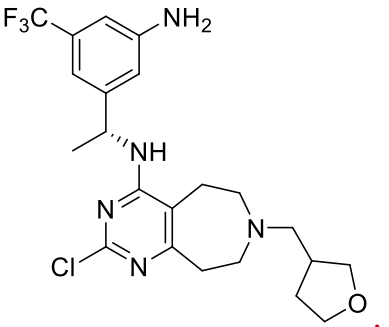
~~19~~12. ~~The compound of claim 1~~A compound, or a pharmaceutically acceptable salt, solvate, stereoisomer, ~~hydrate,~~or tautomer~~, or isomer~~ thereof, selected from the group consisting of the following compounds: ~~of Collection 1~~

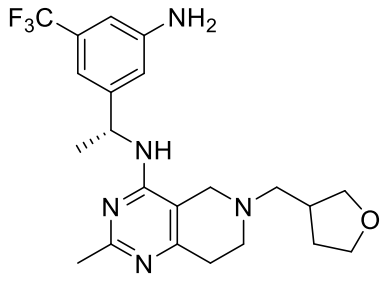
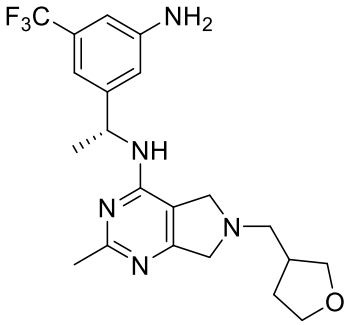
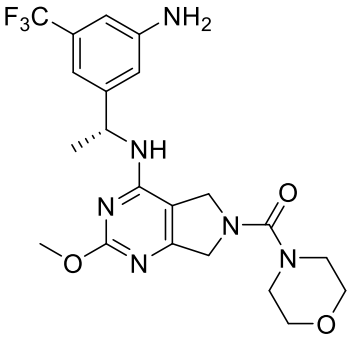



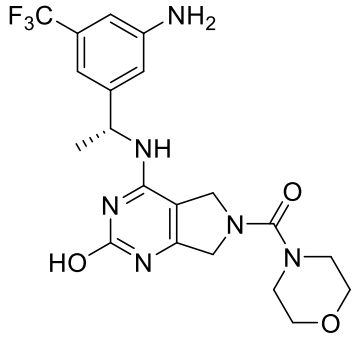
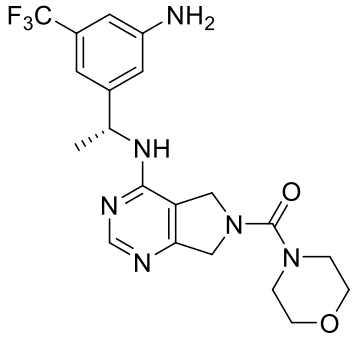
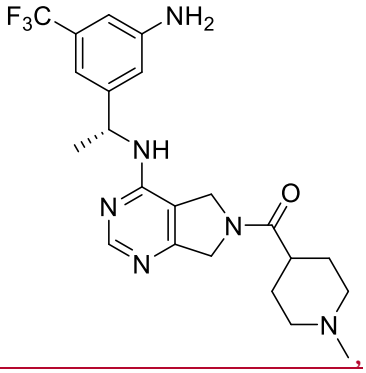




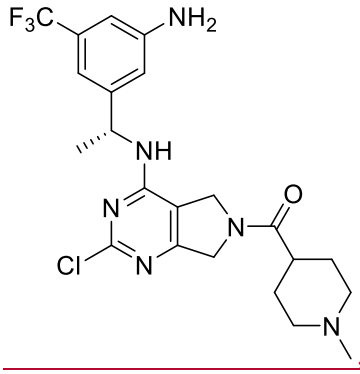
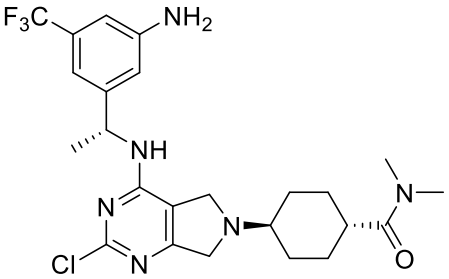



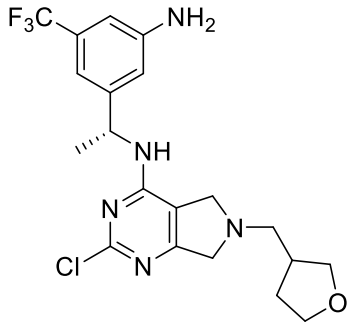
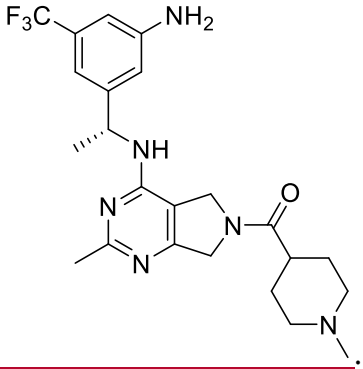



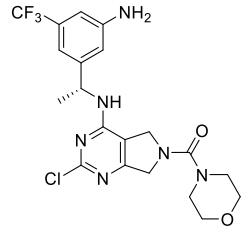
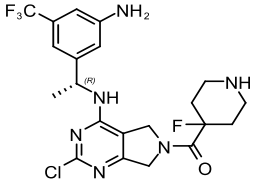
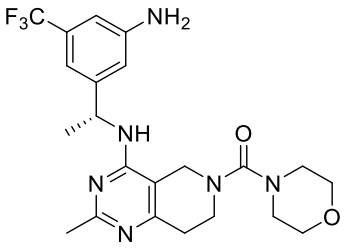
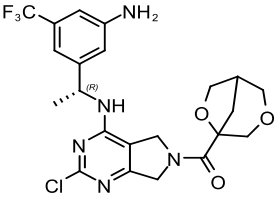
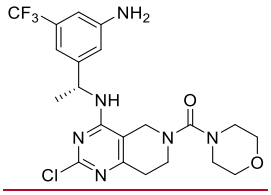
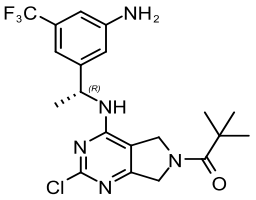
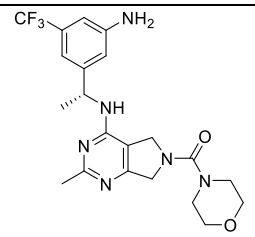
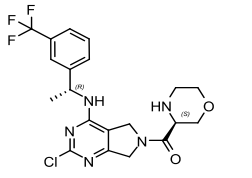
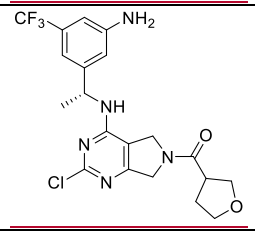
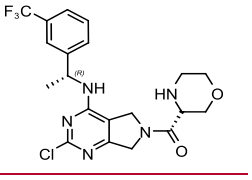
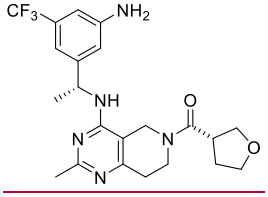
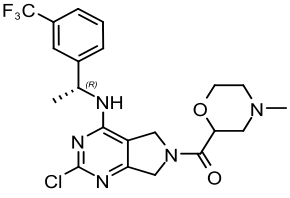



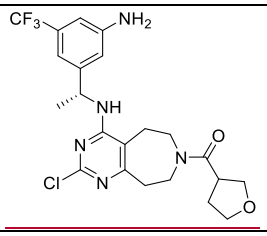
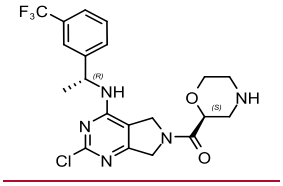
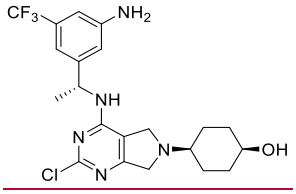
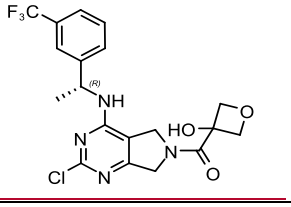
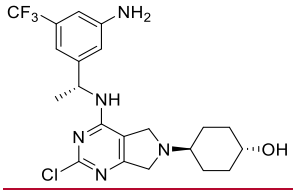
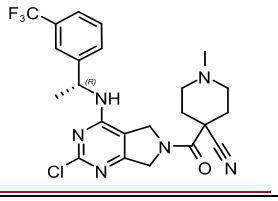
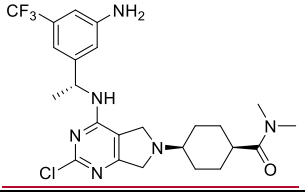
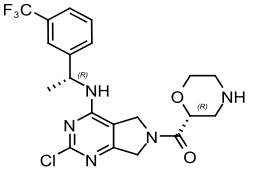
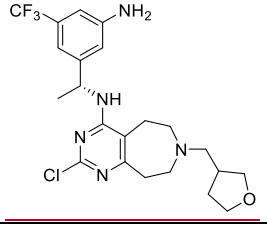
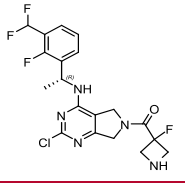
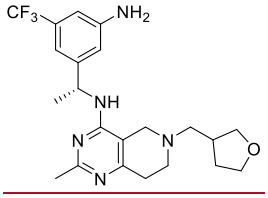
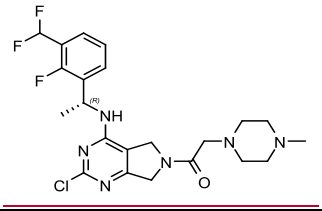
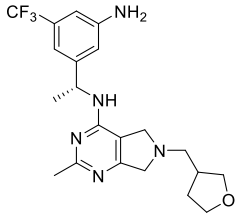
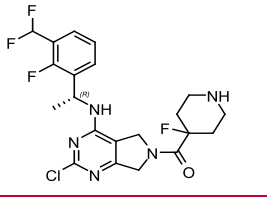
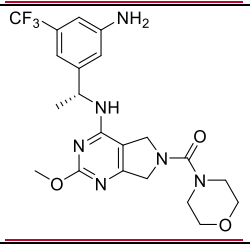
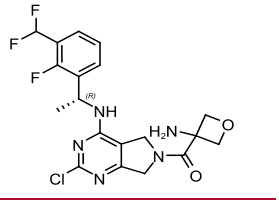
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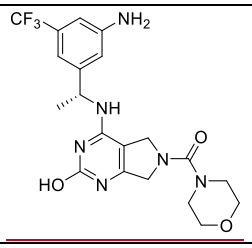
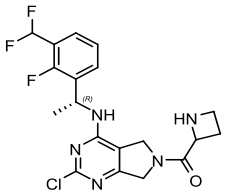
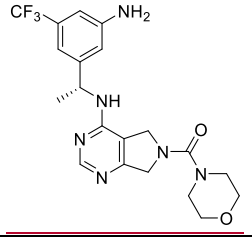
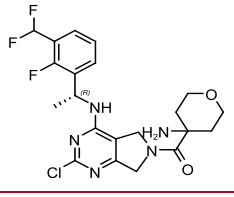
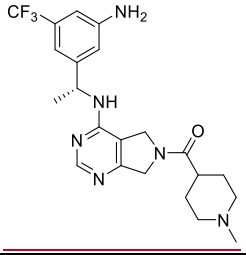
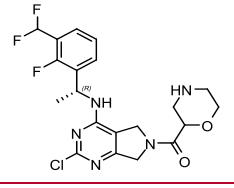
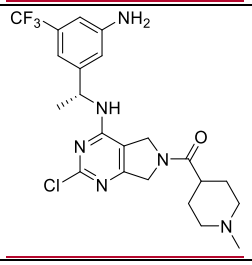
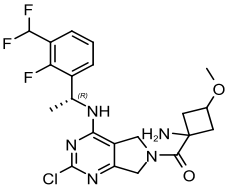
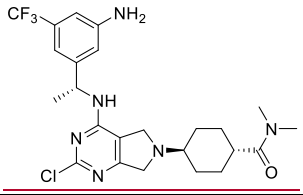
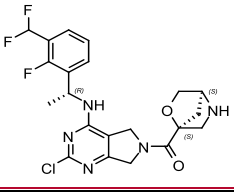
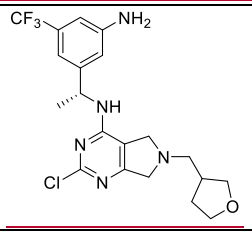
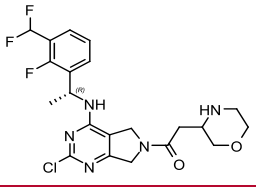
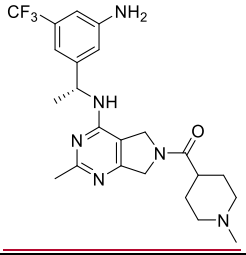
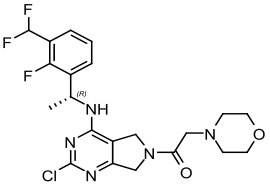
20. ~~The compound of claim 1, or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or isomer thereof, selected from the group consisting of compounds of Collection 2.~~

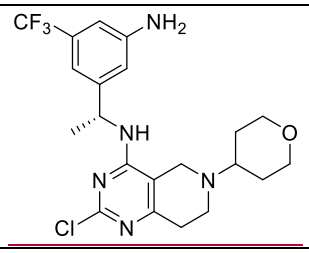
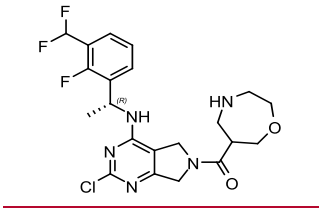
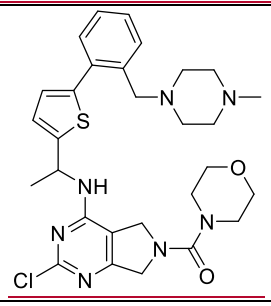
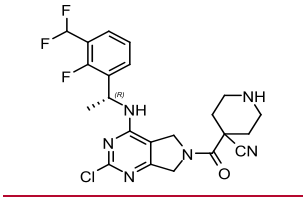
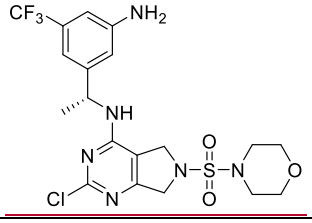
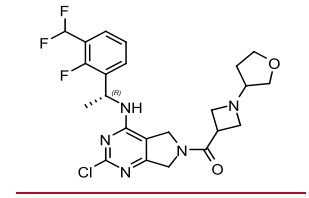
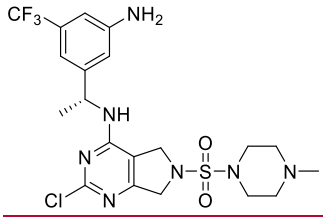
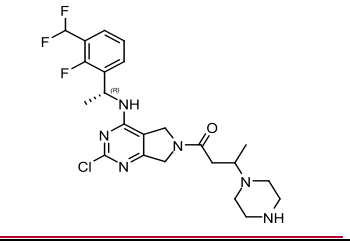
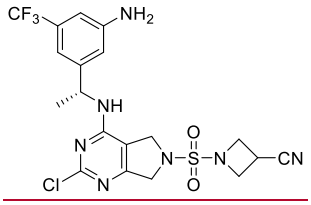
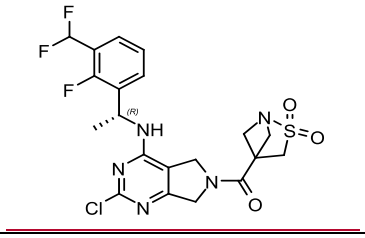
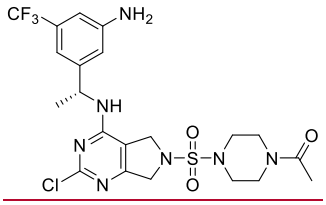
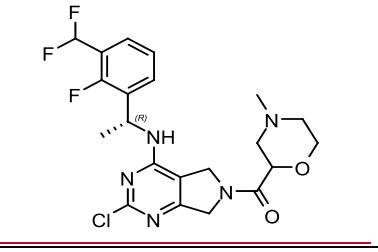
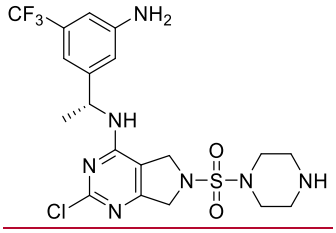
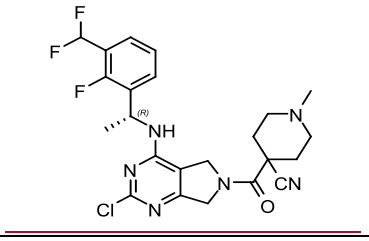
~~21. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or isomer thereof, selected from the group consisting of compounds of Collection 3.~~

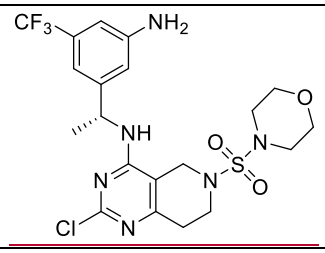
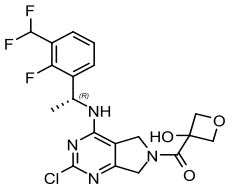
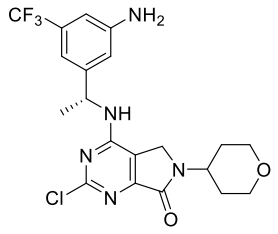
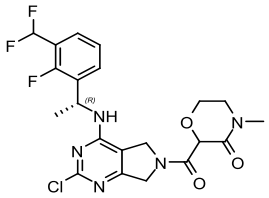
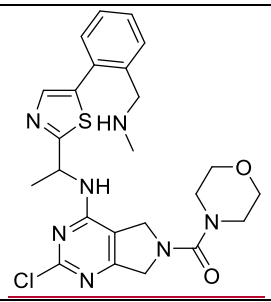
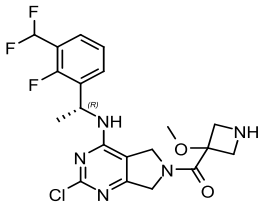
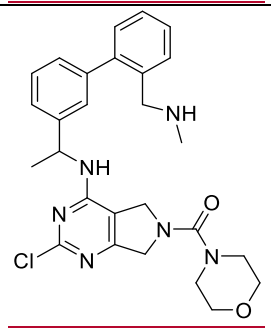
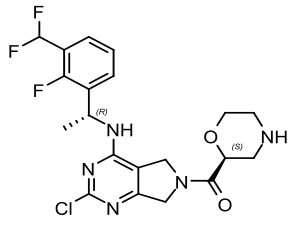
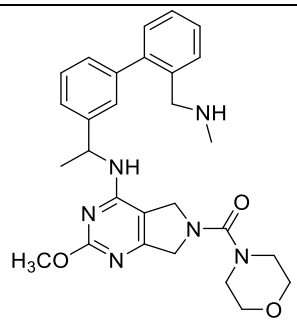
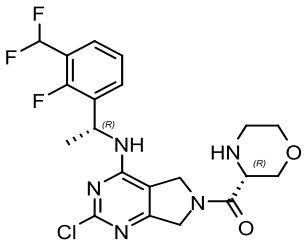
~~22~~13. ~~The compound of claim 1~~A compound, or a pharmaceutically acceptable salt, solvate, stereoisomer, ~~hydrate,~~or tautomer~~, or isomer~~ thereof, selected from the group consisting of compounds shown in the following table ~~of Table A.~~

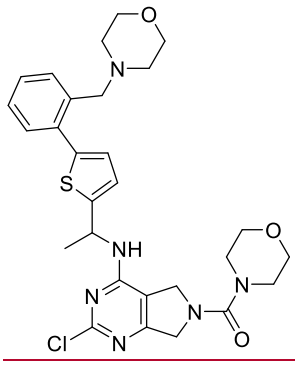
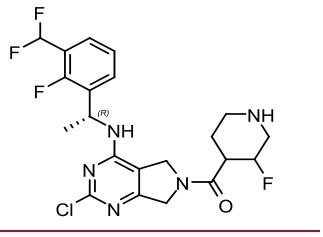
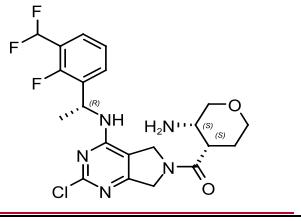
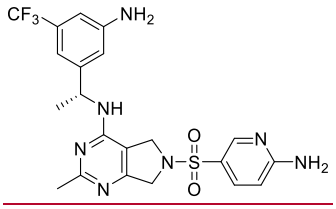
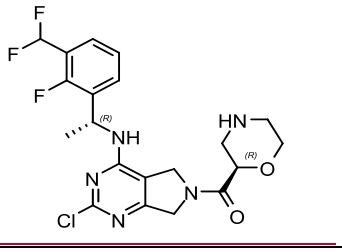
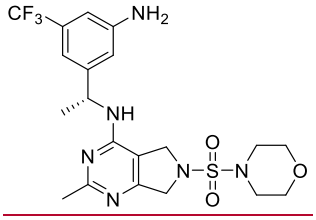
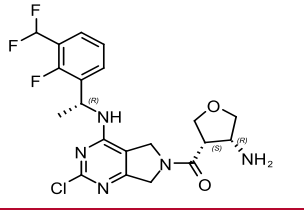
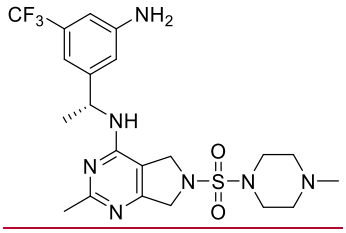
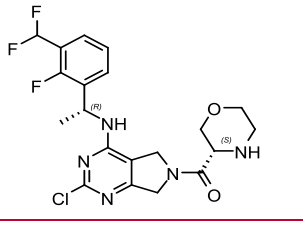
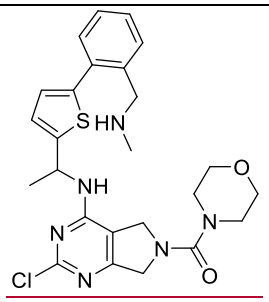
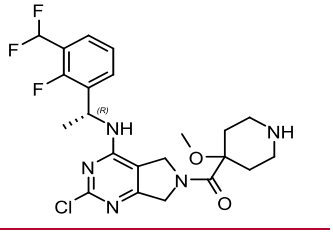
Example #	Structure	Example #	Structure
Example 1.		Example 272.	
Example 2.		Example 273.	
Example 3.		Example 274.	
Example 4.		Example 275.	
Example 5.		Example 276.	
Example 6.		Example 277.	

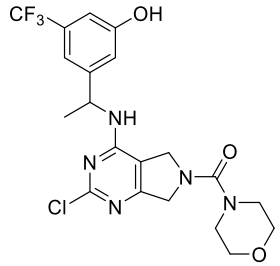
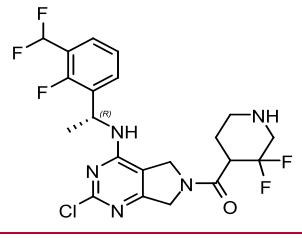
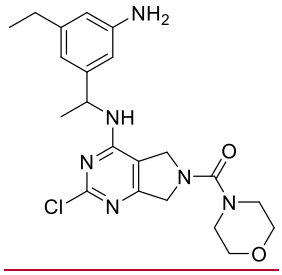
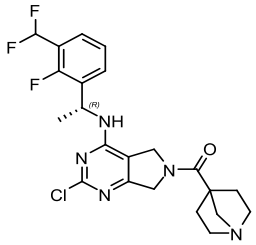
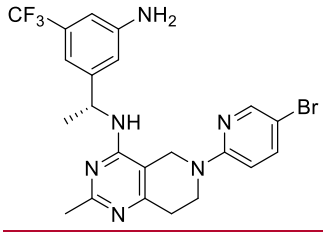
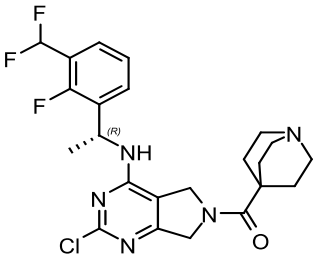
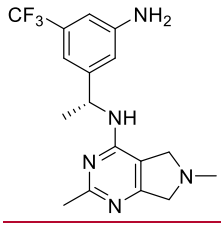
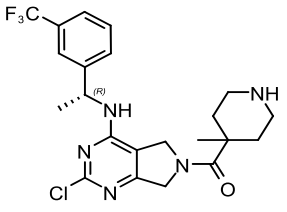
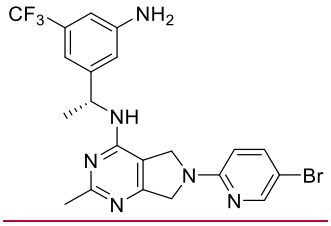
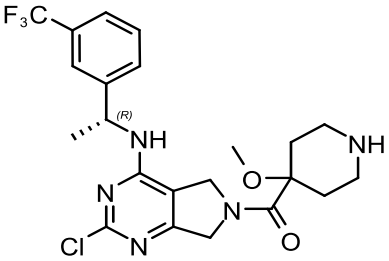
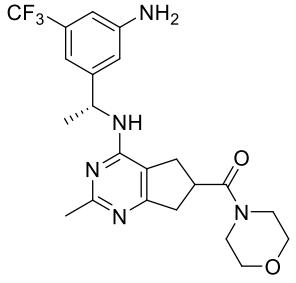
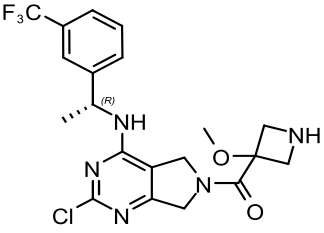
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Example 8.		Example 279.	
Example 9.		Example 280.	
Example 10.		Example 281.	
Example 11.		Example 282.	
Example 12.		Example 283.	
Example 13.		Example 284.	
Example 14.		Example 285.	

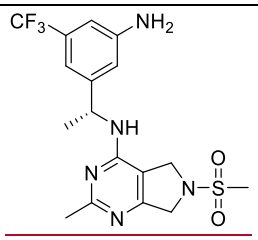
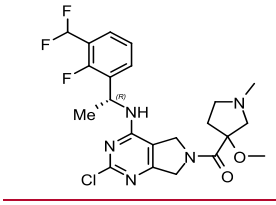
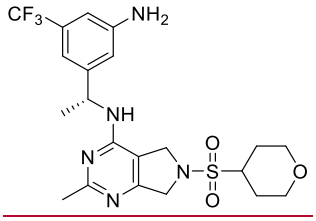
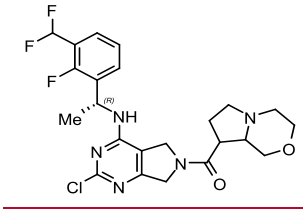
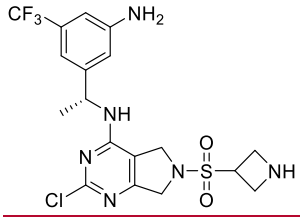
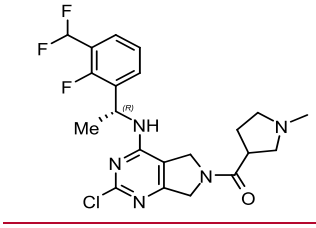
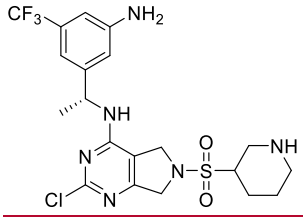
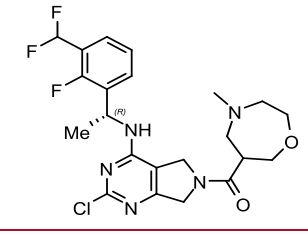
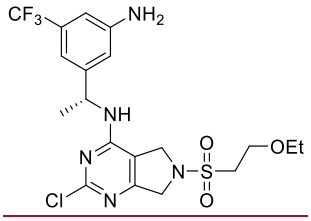
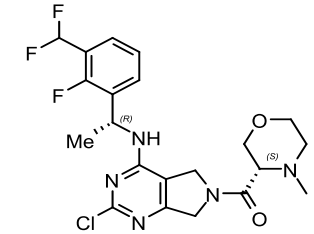
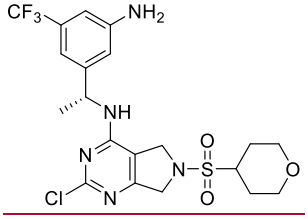
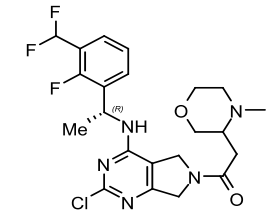
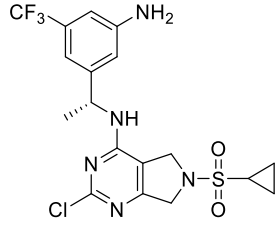
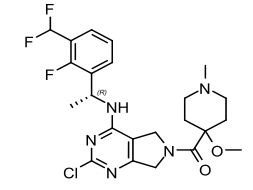
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Example 16.		Example 287.	
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Example 18.		Example 289.	
Example 19.		Example 290.	
Example 20.		Example 291.	
Example 21.		Example 292.	

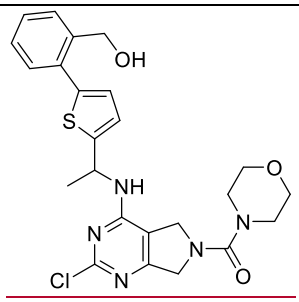
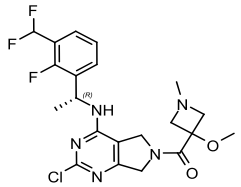
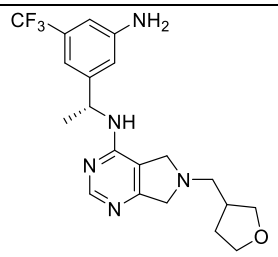
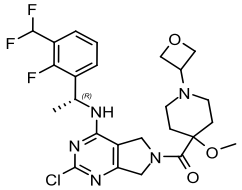
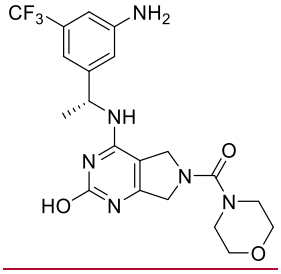
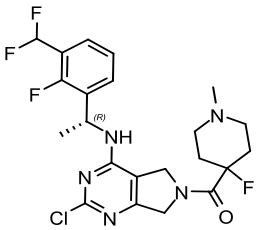
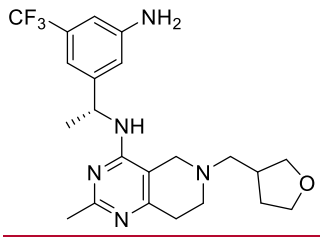
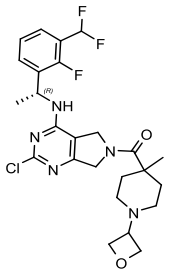
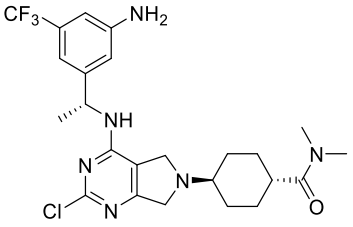
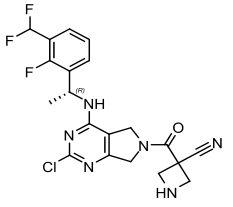
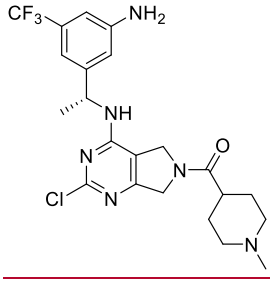
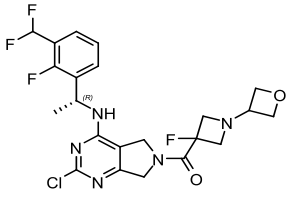
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Example 23.		Example 294.	
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Example 25.		Example 296.	
Example 26.		Example 297.	
Example 27.		Example 298.	
Example 28.		Example 299.	

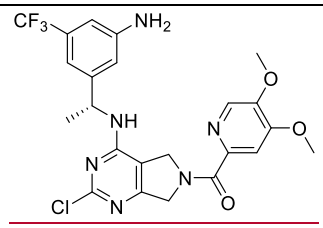
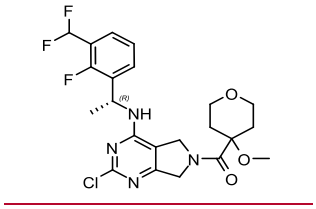
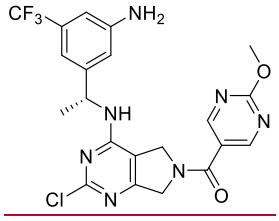
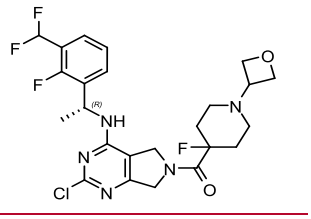
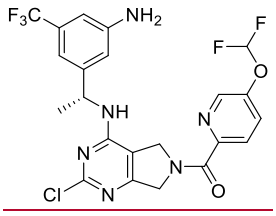
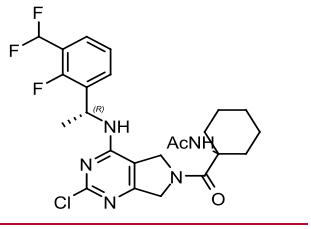
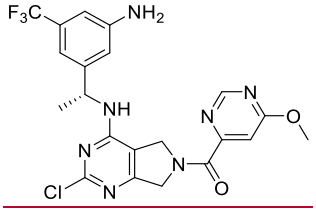
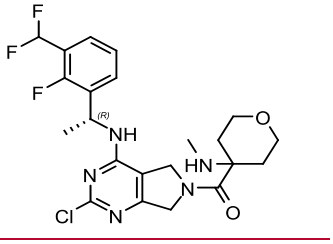
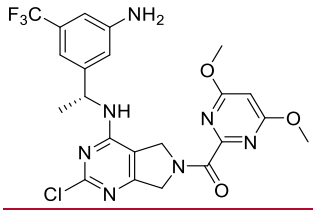
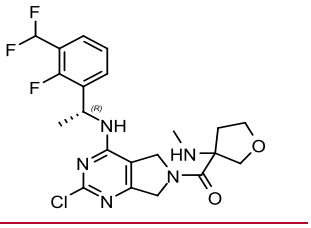
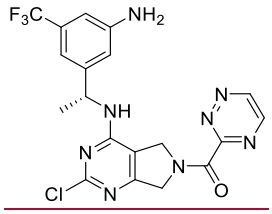
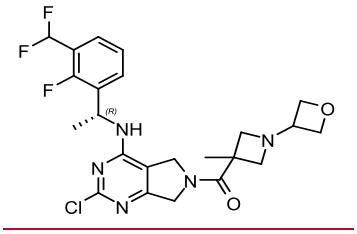
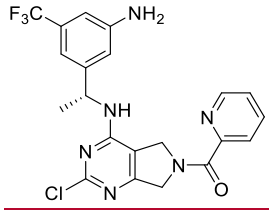
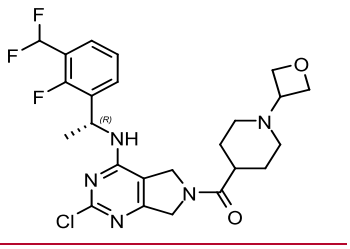
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Example 31.		Example 302.	
Example 32.		Example 303.	
Example 33.		Example 304.	

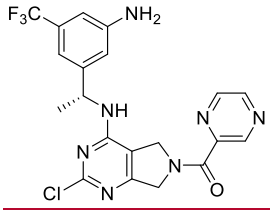
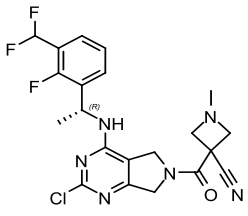
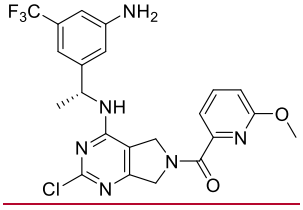
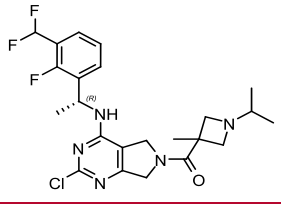
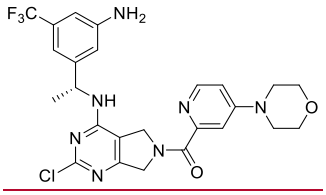
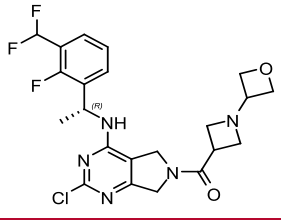
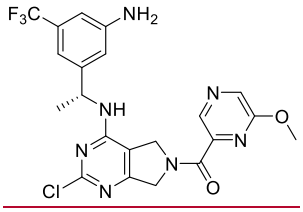
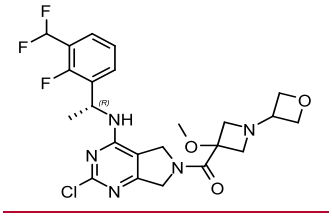
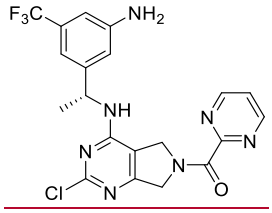
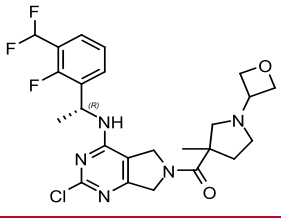
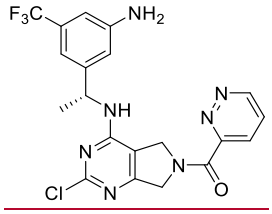
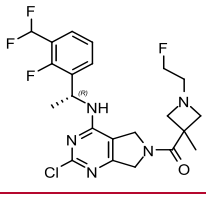
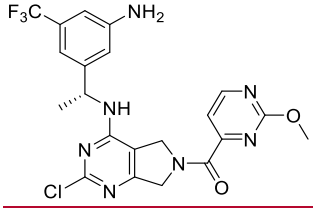
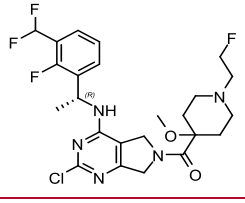
Example 34.		Example 305.	
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Example 36.		Example 307.	
Example 37.		Example 308.	
Example 38.		Example 309.	
Example 39.		Example 310.	

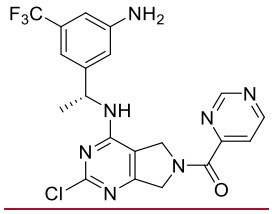
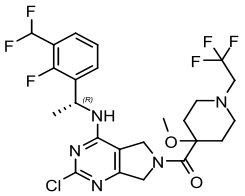
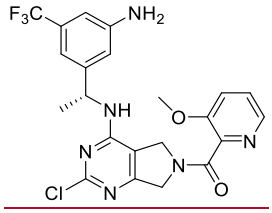
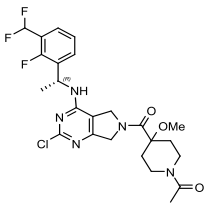
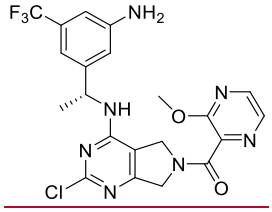
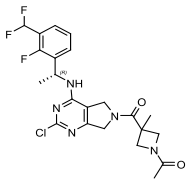
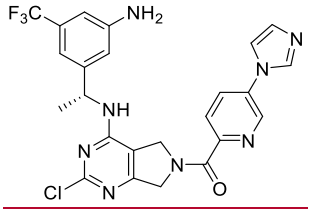
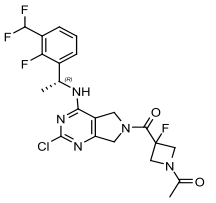
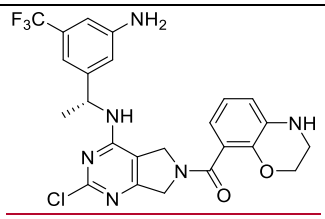
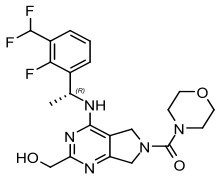
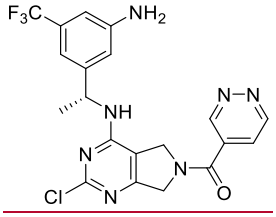
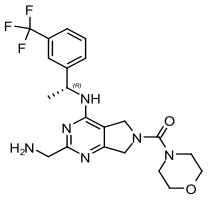
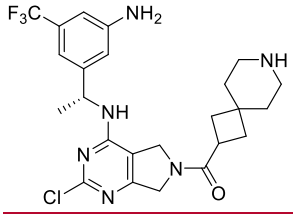
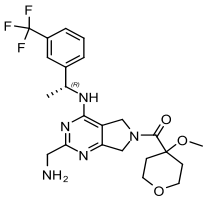
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Example 43.		Example 314.	
Example 44.		Example 315.	
Example 45.		Example 316.	

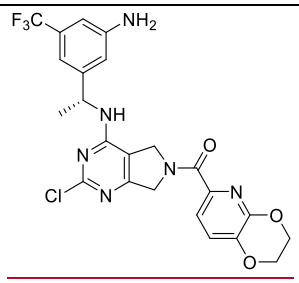
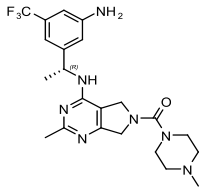
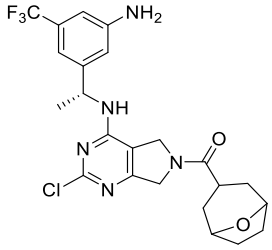
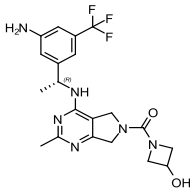
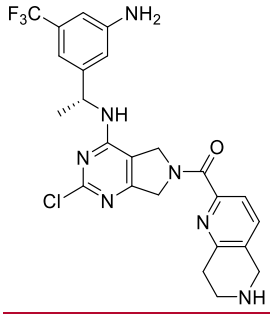
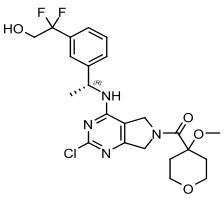
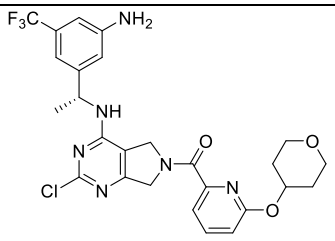
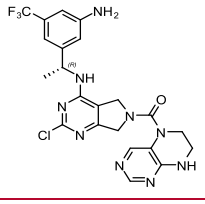
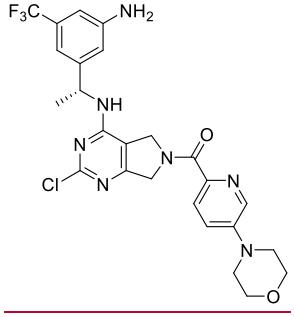
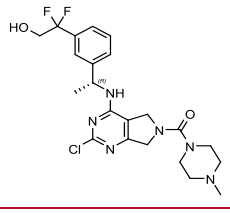
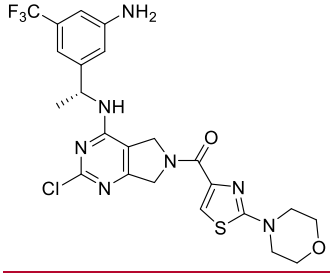
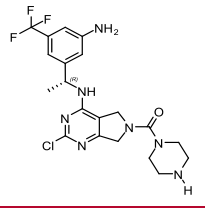
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Example 47.		Example 318.	
Example 48., 166.		Example 319.	
Example 49.		Example 320.	
Example 50.		Example 321.	
Example 51.		Example 322.	
Example 52.		Example 323.	

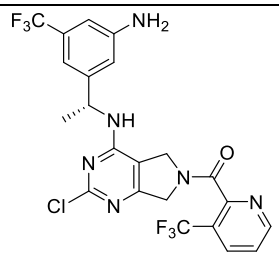
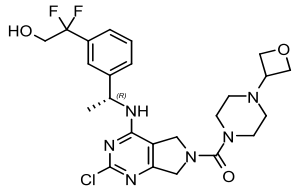
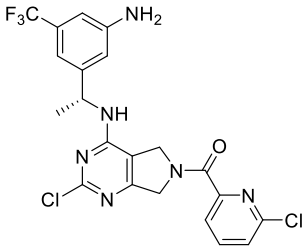
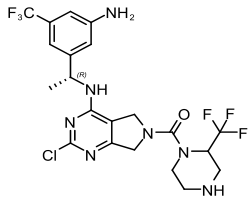
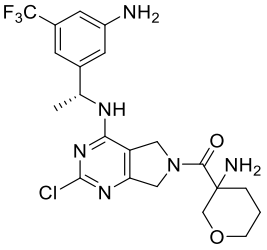
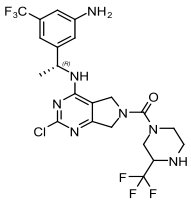
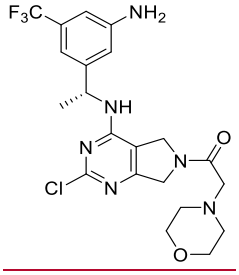
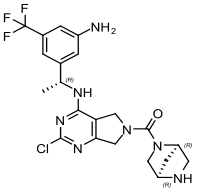
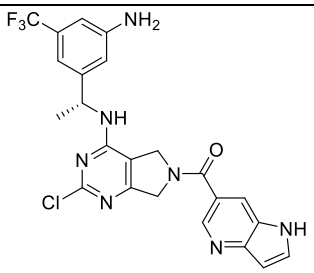
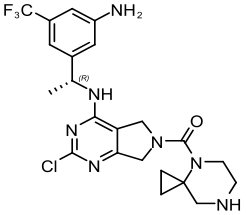
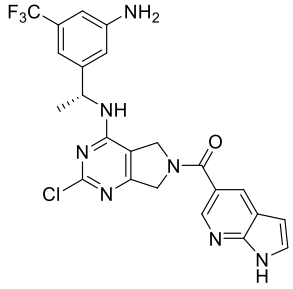
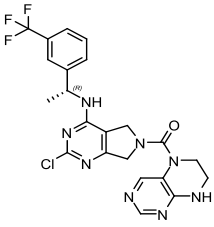
Example 53.		Example 324.	
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Example 55.		Example 326.	
Example 56.		Example 327.	
Example 57.		Example 328.	
Example 58.		Example 329.	

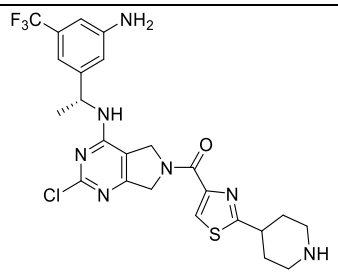
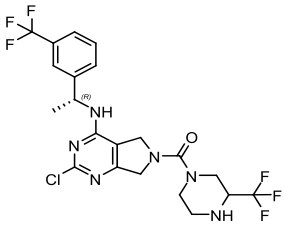
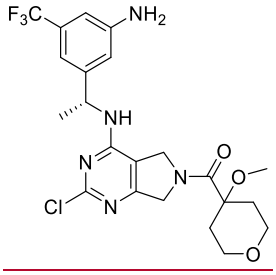
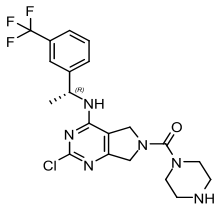
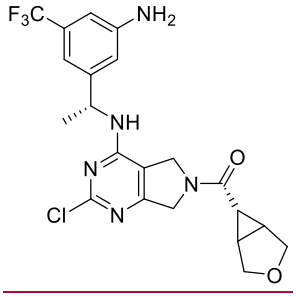
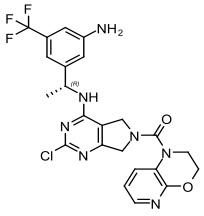
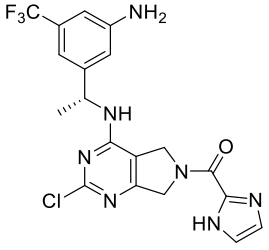
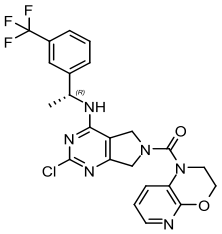
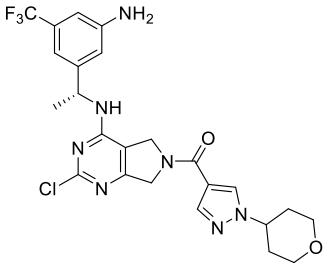
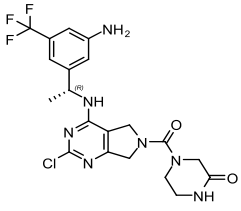
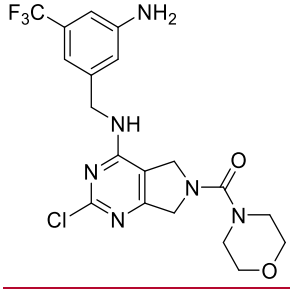
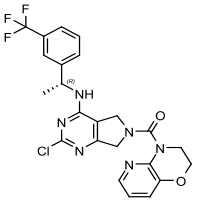
Example 59.		Example 330.	
Example 60.		Example 331.	
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Example 62.		Example 333.	
Example 63.		Example 334.	
Example 64.		Example 335.	
Example 65.		Example 336.	

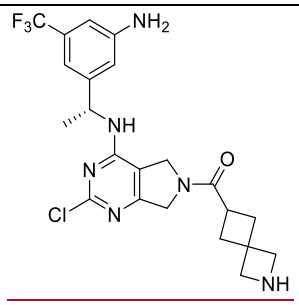
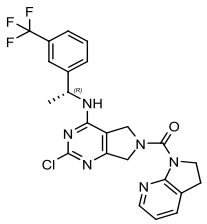
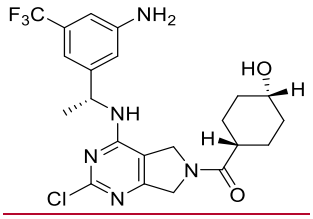
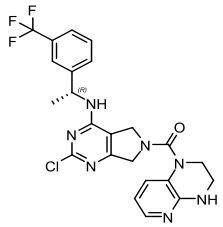
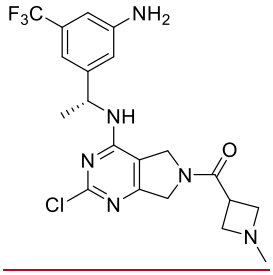
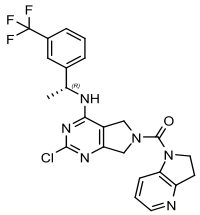
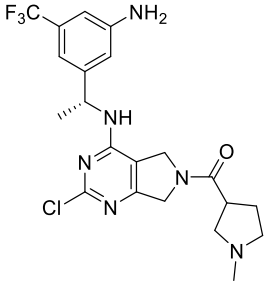
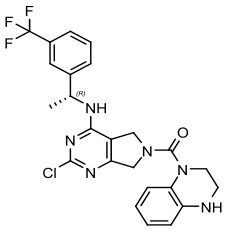
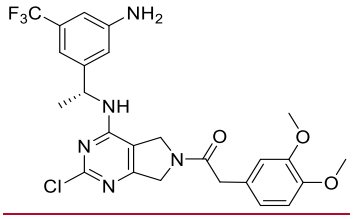
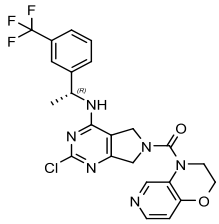
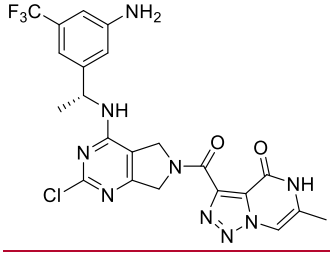
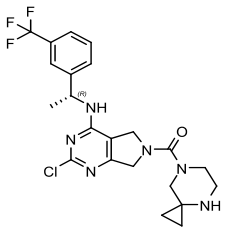
Example 66.		Example 337.	
Example 67.		Example 338.	
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Example 69.		Example 340.	
Example 70.		Example 341.	
Example 71.		Example 342.	
Example 72.		Example 343.	

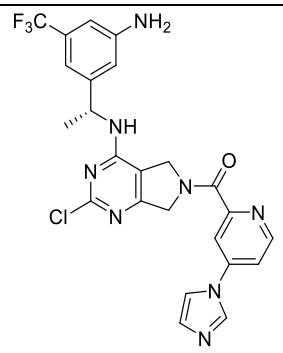
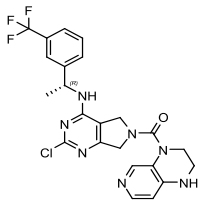
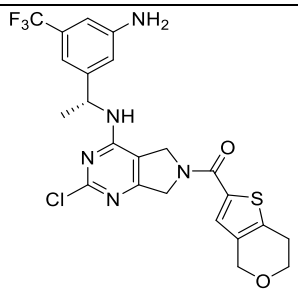
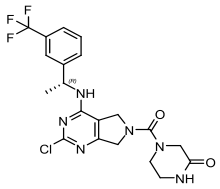
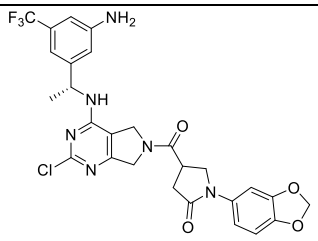
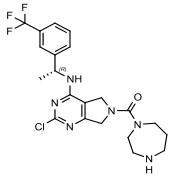
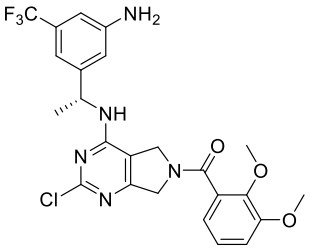
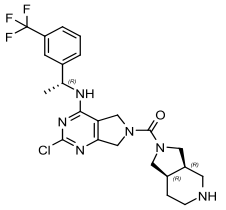
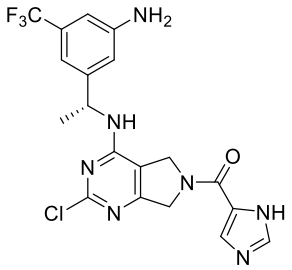
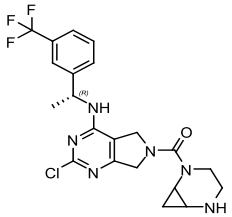
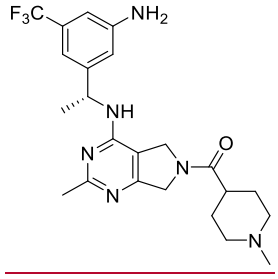
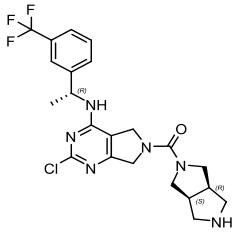
Example 73.		Example 344.	
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Example 77.		Example 348.	
Example 78.		Example 349.	
Example 79.		Example 350.	

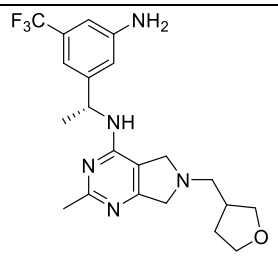
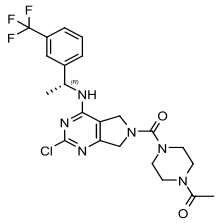
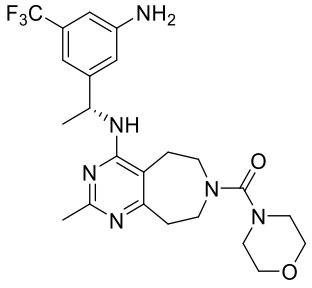
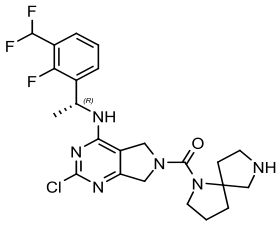
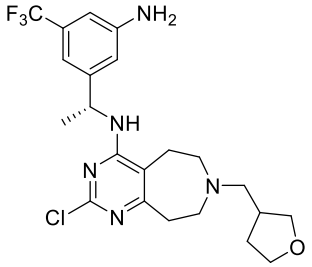
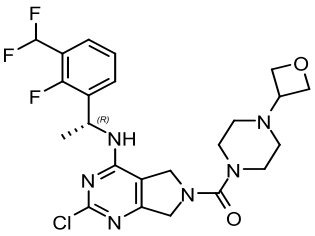
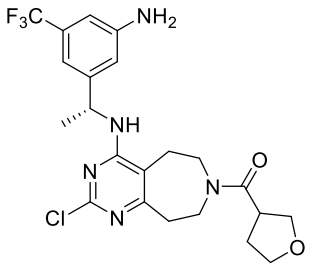
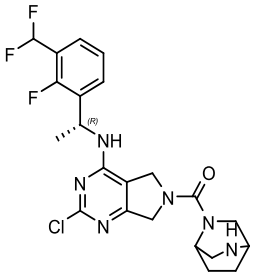
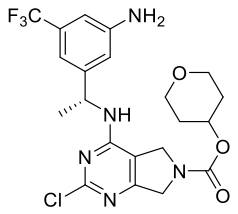
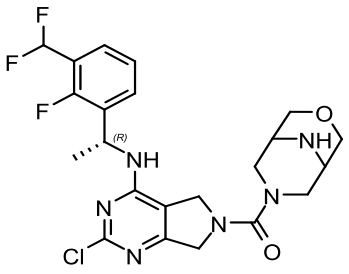
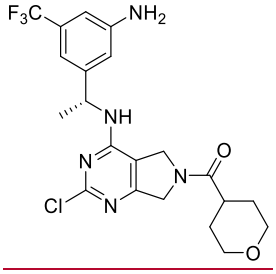
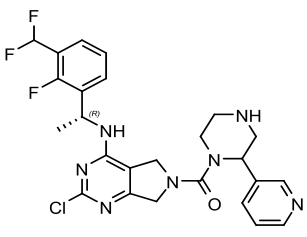
Example 80.		Example 351.	
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Example 84.		Example 355.	
Example 85.		Example 356.	

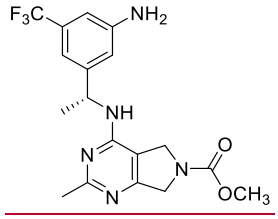
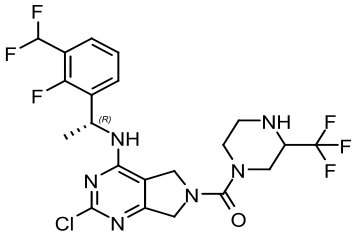
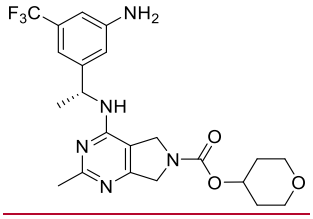
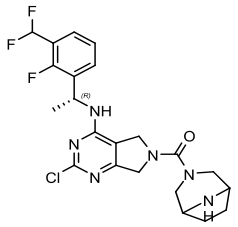
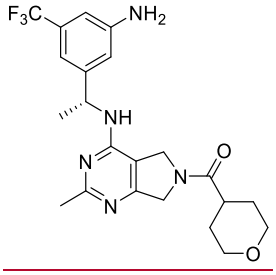
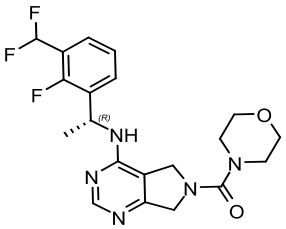
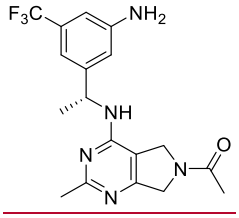
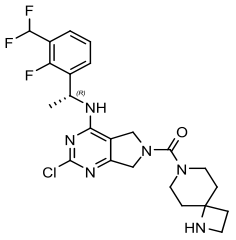
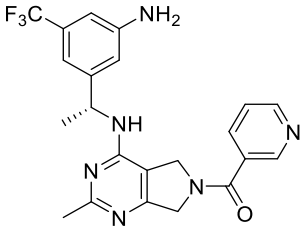
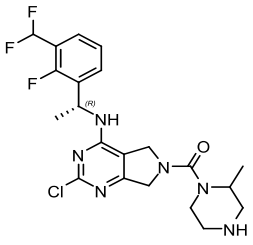
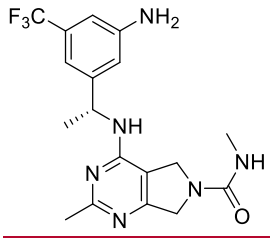
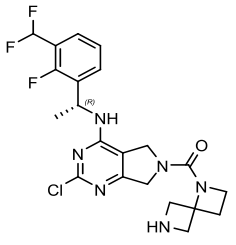
Example 86.		Example 357.	
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Example 89.		Example 360.	
Example 90.		Example 361.	
Example 91.		Example 362.	

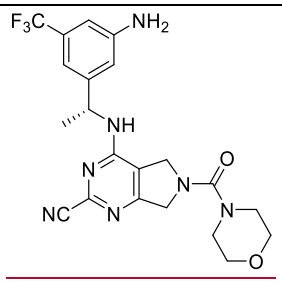
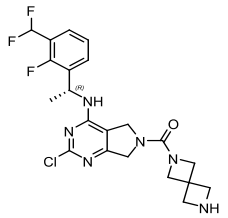
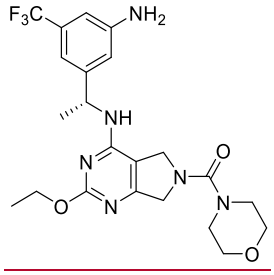
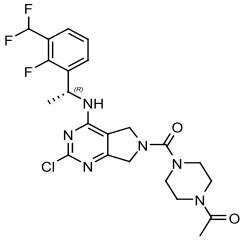
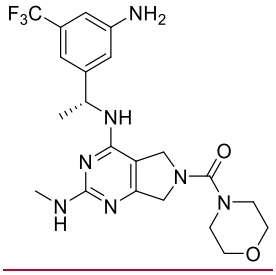
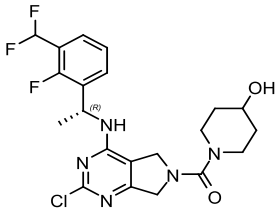
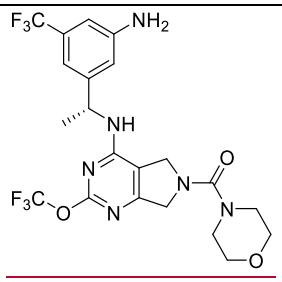
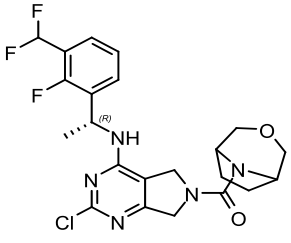
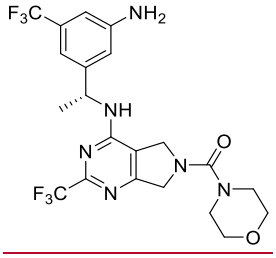
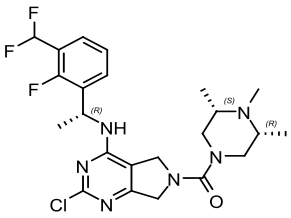
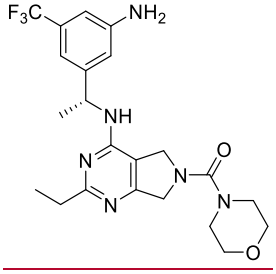
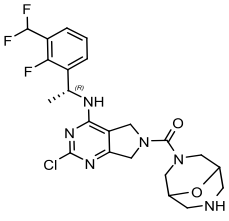
Example 92.		Example 363.	
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Example 94.		Example 365.	
Example 95.		Example 366.	
Example 96.		Example 367.	
Example 97.		Example 368.	

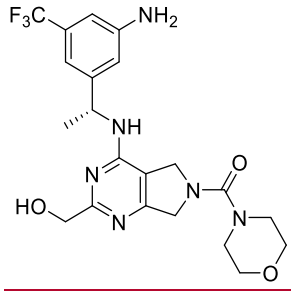
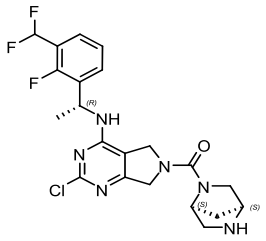
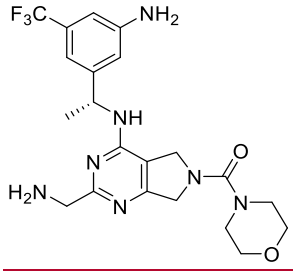
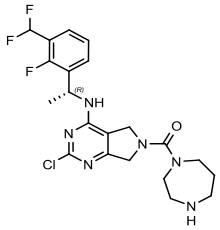
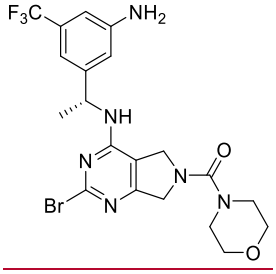
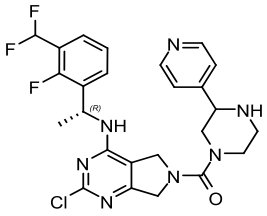
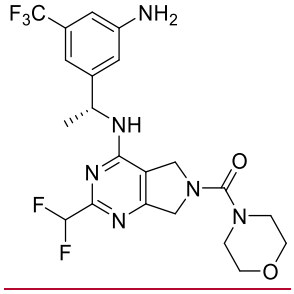
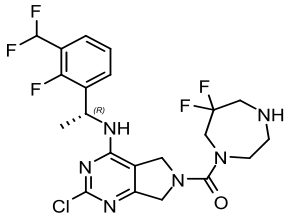
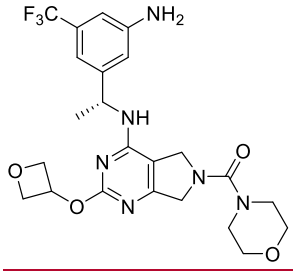
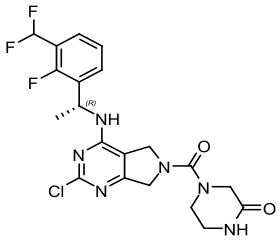
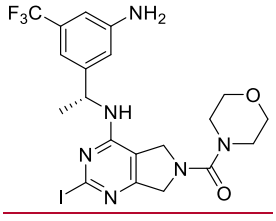
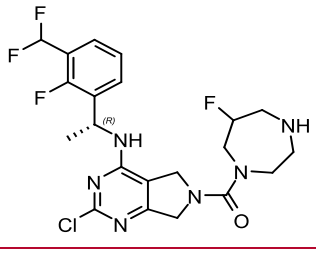
Example 98.		Example 369.	
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Example 100.		Example 371.	
Example 101.		Example 372.	
Example 102.		Example 373.	
Example 103.		Example 374.	

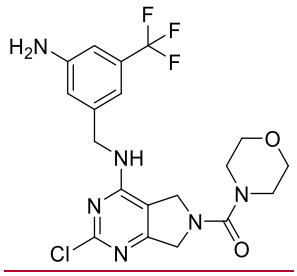
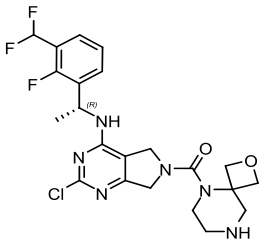
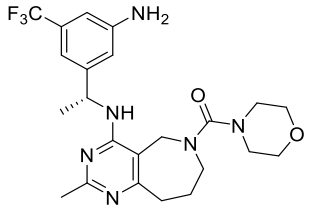
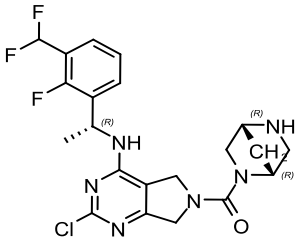
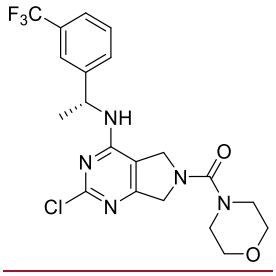
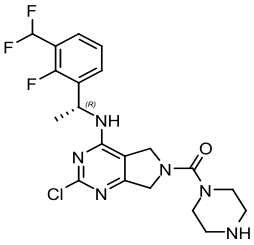
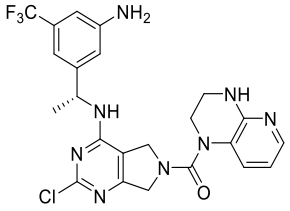
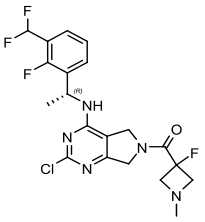
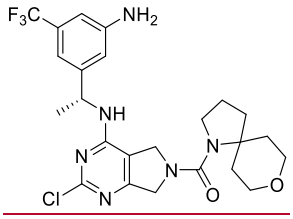
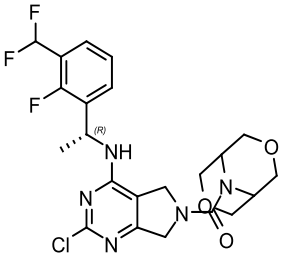
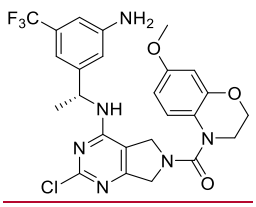
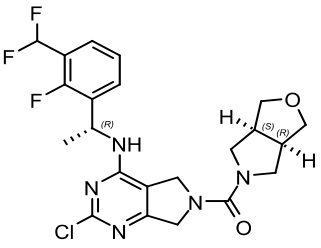
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Example 106.		Example 377.	
Example 107.		Example 378.	
Example 108.		Example 379.	
Example 109.		Example 380.	

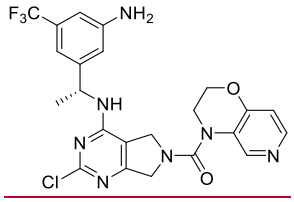
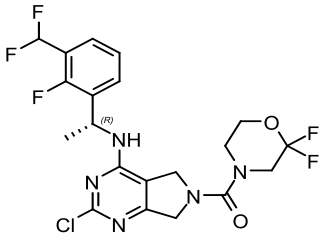
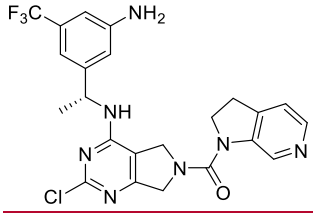
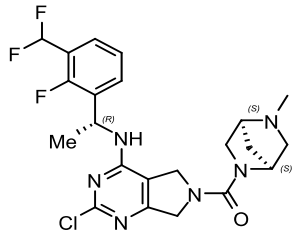
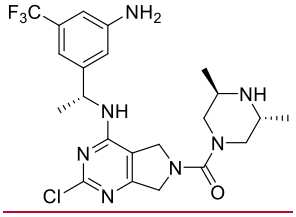
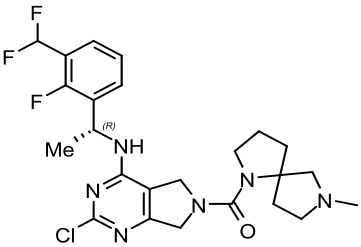
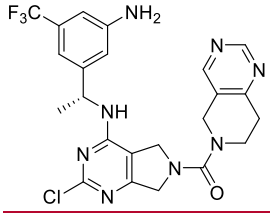
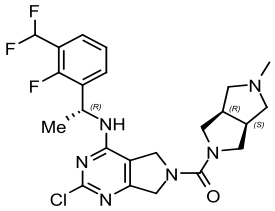
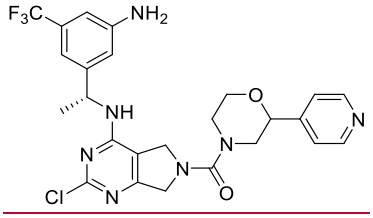
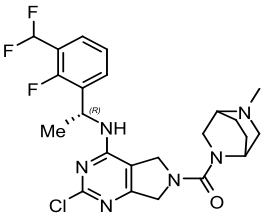
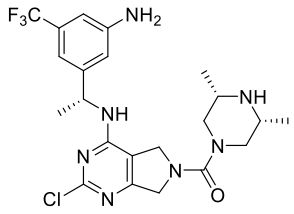
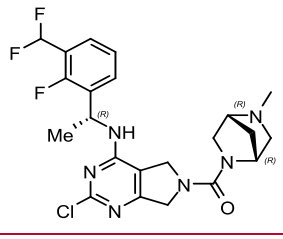
Example 111.		Example 381.	
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Example 113.		Example 383.	
Example 114.		Example 384.	
Example 115.		Example 385.	
Example 116.		Example 386.	

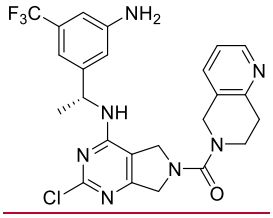
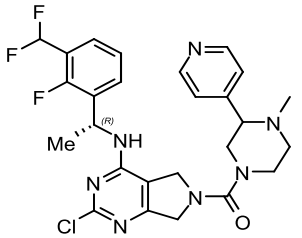
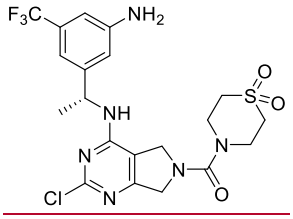
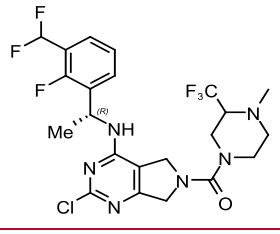
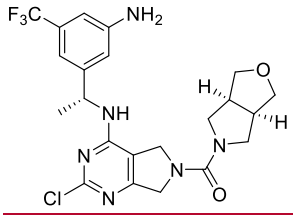
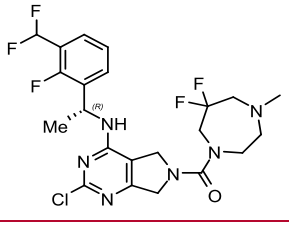
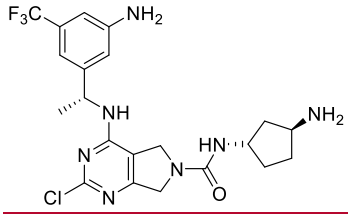
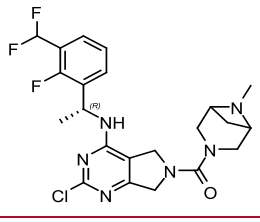
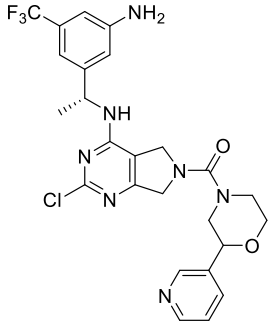
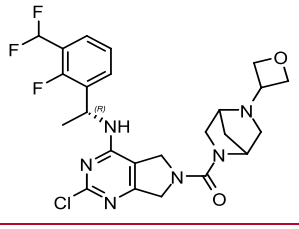
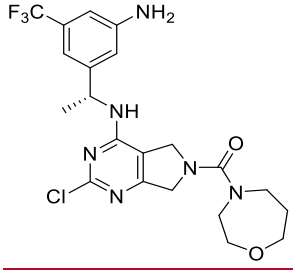
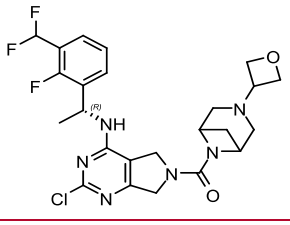
Example 117.		Example 387.	
Example 118.		Example 388.	
Example 119.		Example 389.	
Example 120.		Example 390.	
Example 121.		Example 391.	
Example 122.		Example 392.	

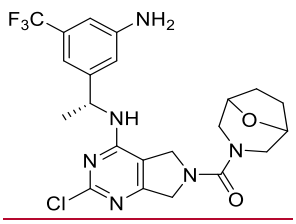
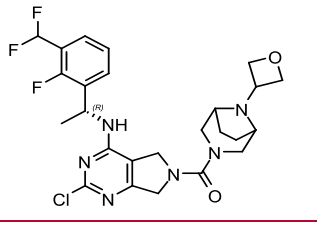
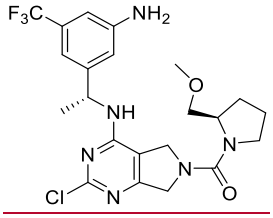
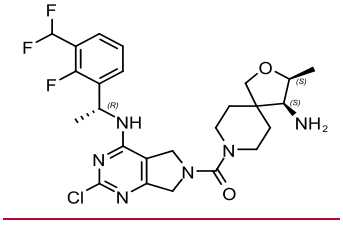
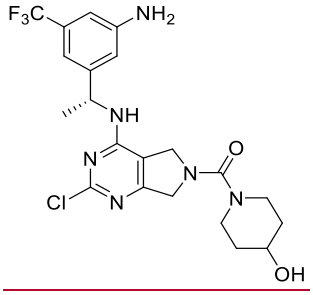
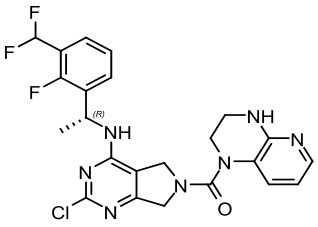
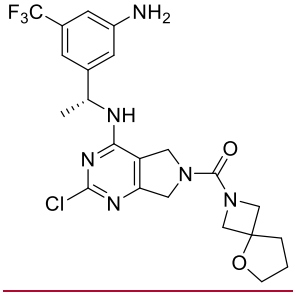
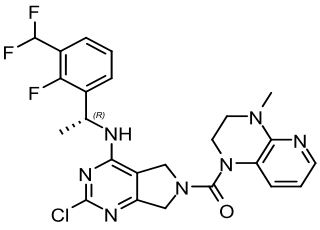
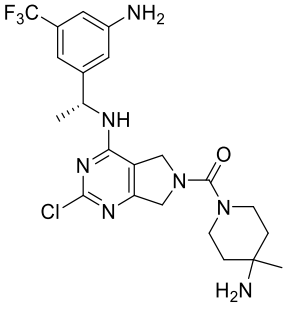
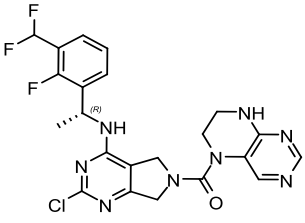
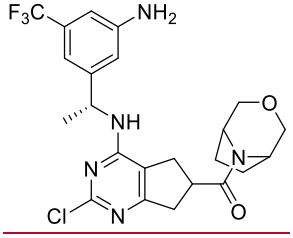
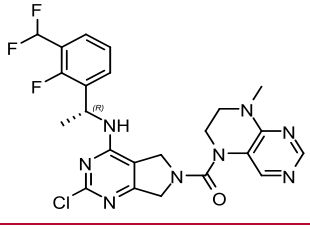
Example 123.		Example 393.	
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Example 125.		Example 395.	
Example 126.		Example 396.	
Example 127.		Example 397.	
Example 128.		Example 398.	

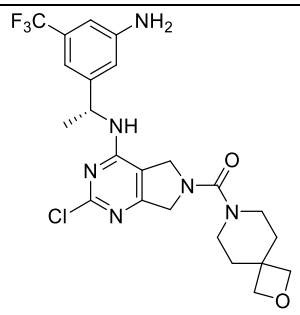
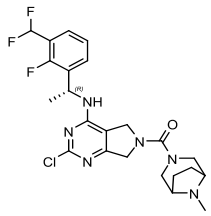
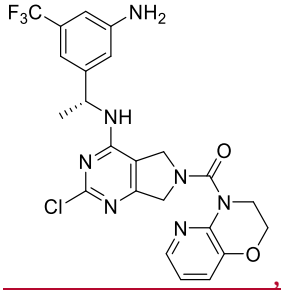
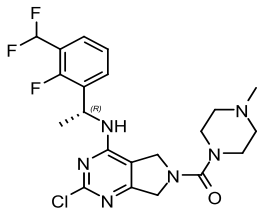
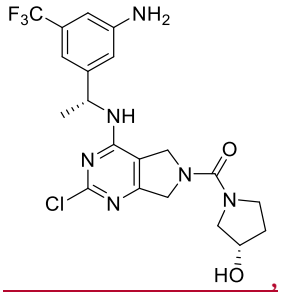
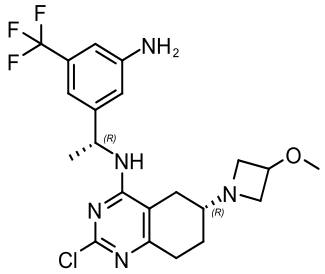
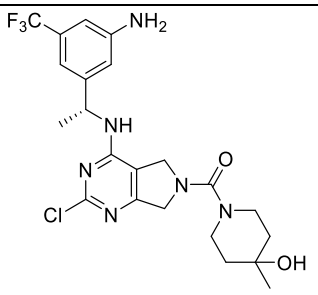
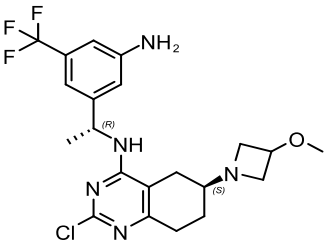
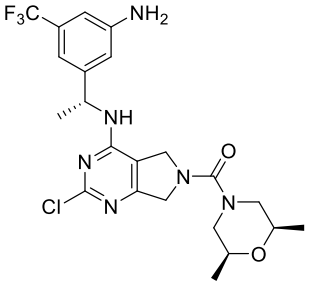
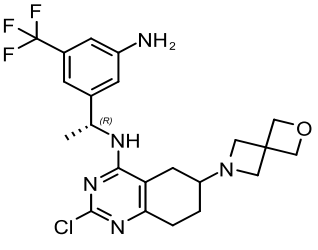
Example 129.		Example 399.	
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Example 132.		Example 402.	
Example 133.		Example 403.	
Example 134.		Example 404.	

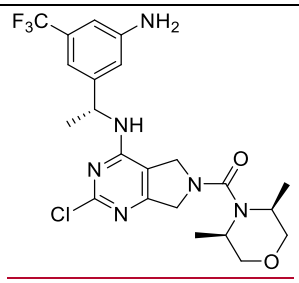
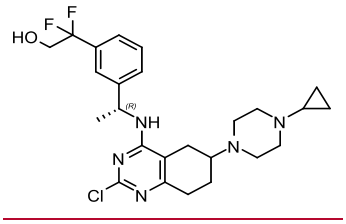
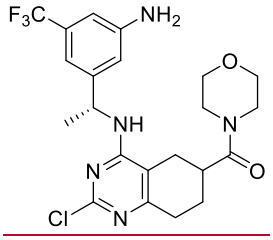
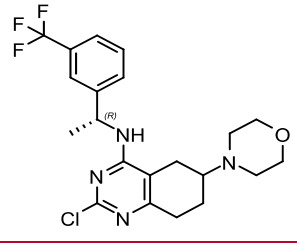
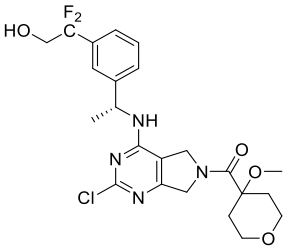
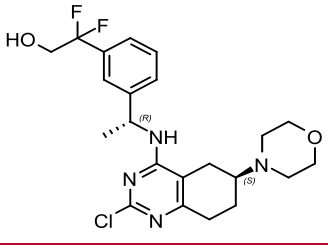
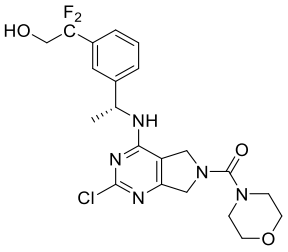
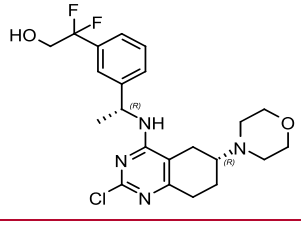
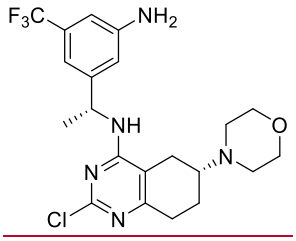
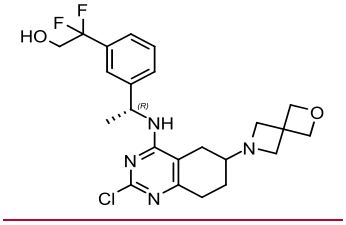
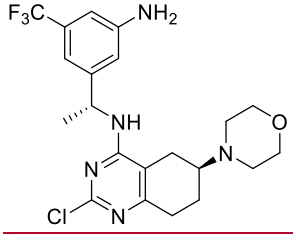
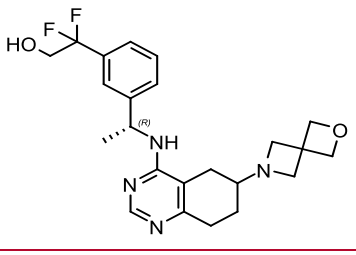
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Example 138.		Example 408.	
Example 139.		Example 409.	
Example 140.		Example 410.	

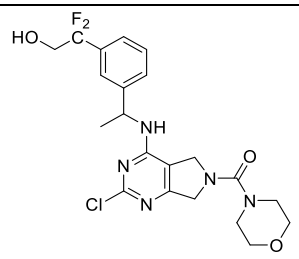
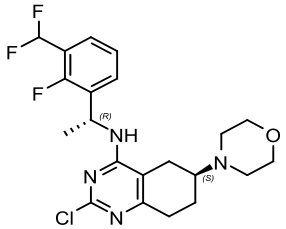
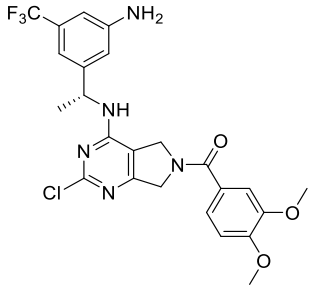
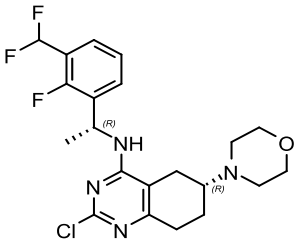
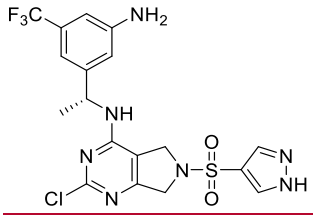
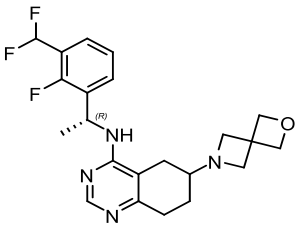
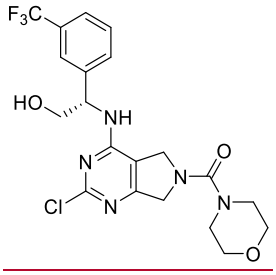
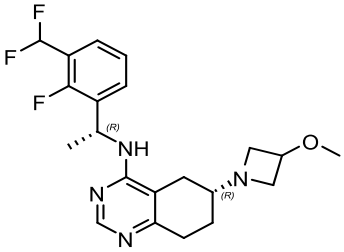
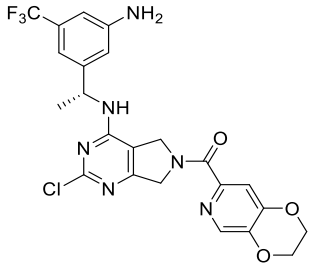
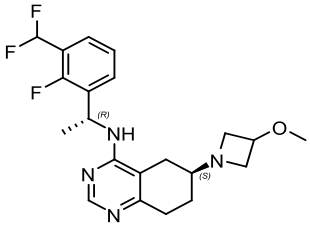
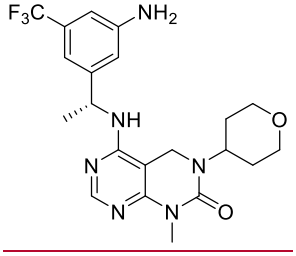
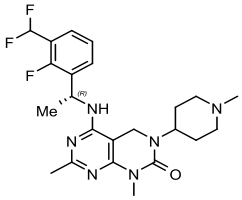
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Example 144.		Example 414.	
Example 145.		Example 415.	
Example 146.		Example 416.	

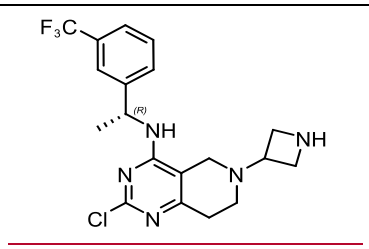
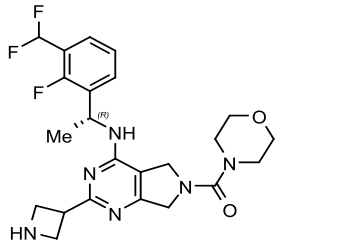
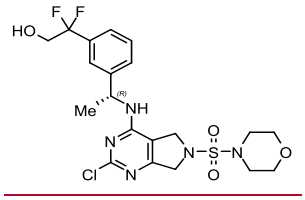
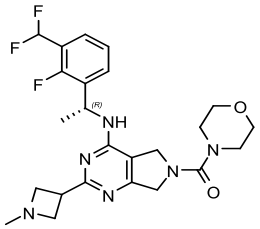
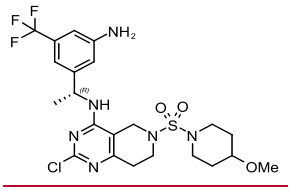
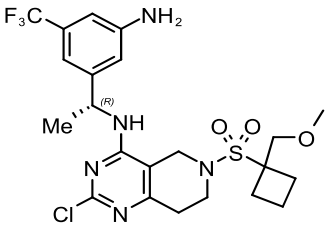
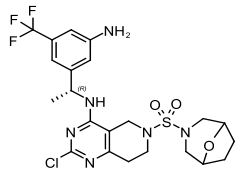
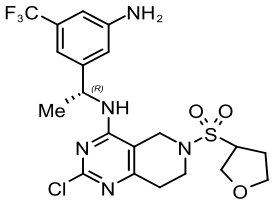
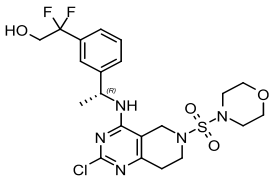
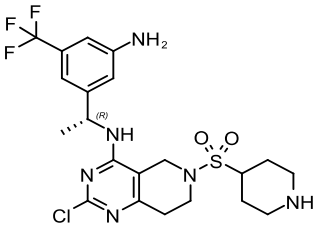
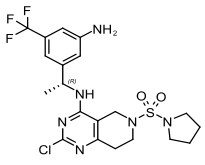
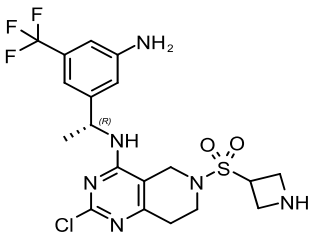
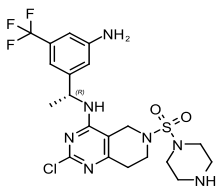
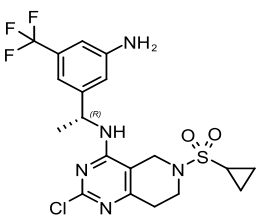
Example 147.		Example 417.	
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Example 150.		Example 420.	
Example 151.		Example 421.	
Example 152.		Example 422.	

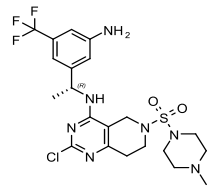
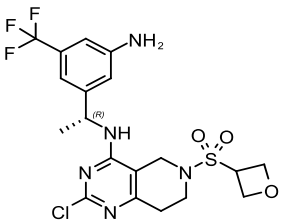
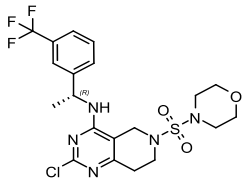
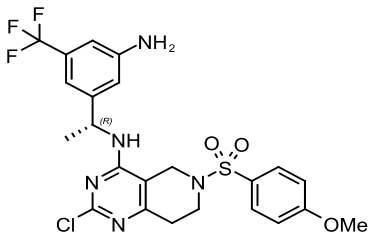
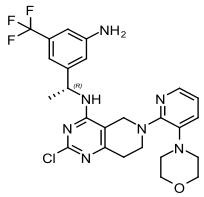
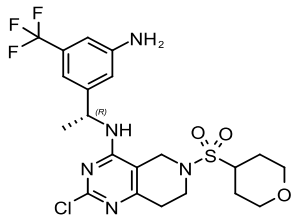
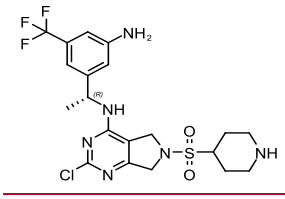
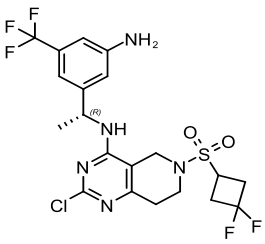
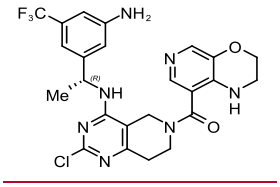
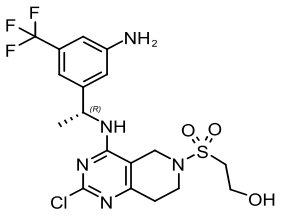
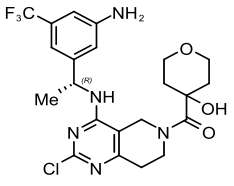
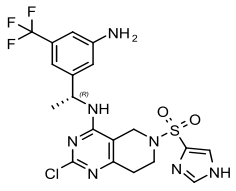
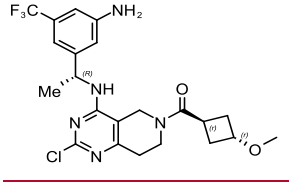
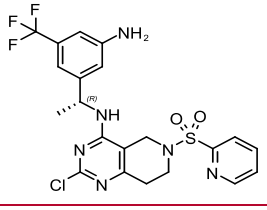
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Example 157.		Example 427.	
Example 158.		Example 428.	

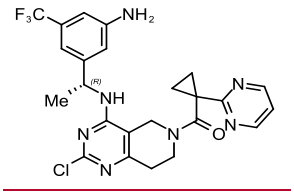
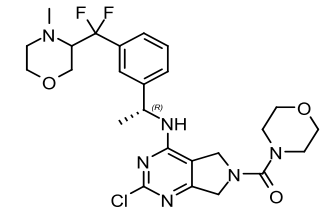
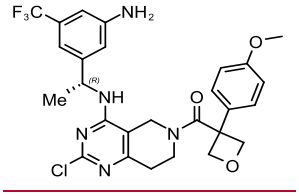
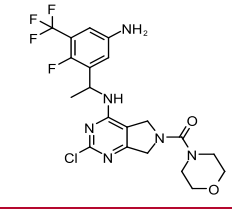
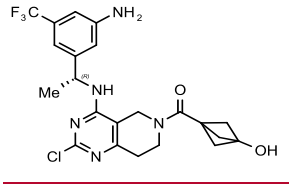
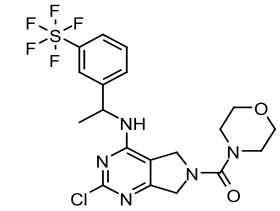
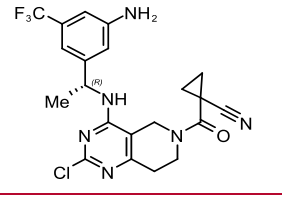
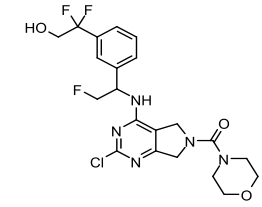
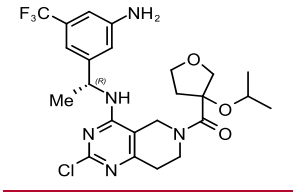
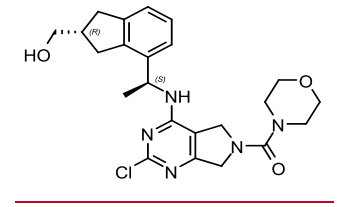
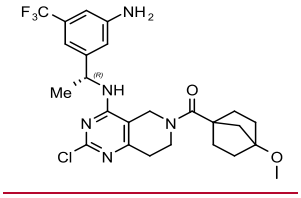
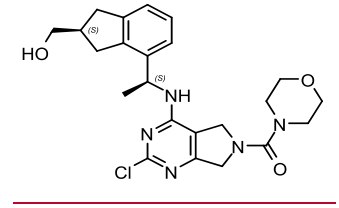
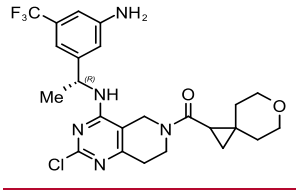
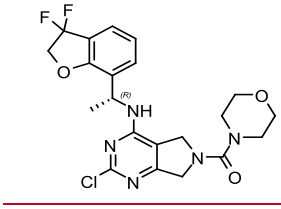
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Example 162.		Example 432.	
Example 163.		Example 433.	

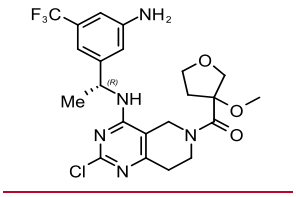
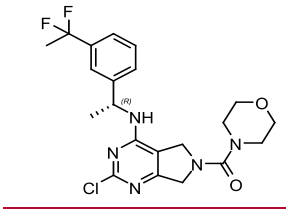
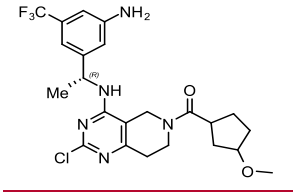
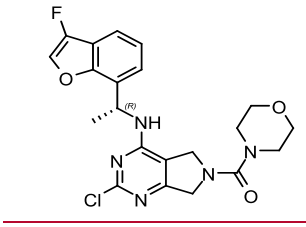
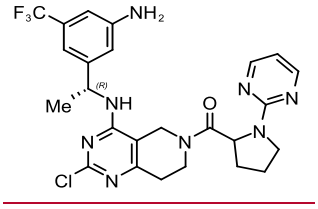
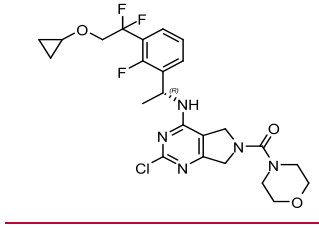
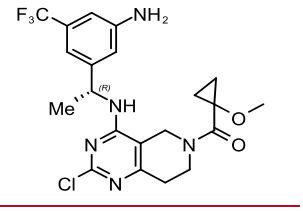
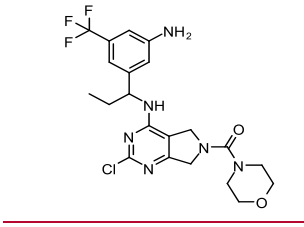
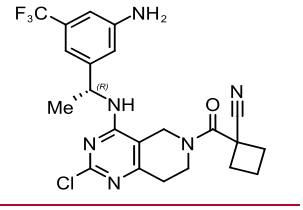
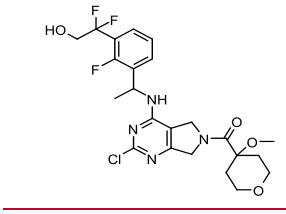
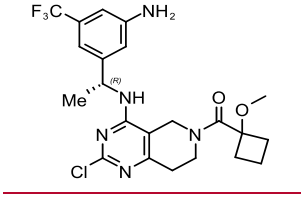
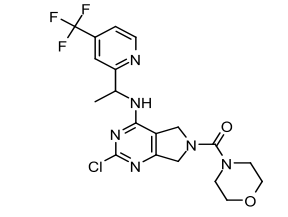
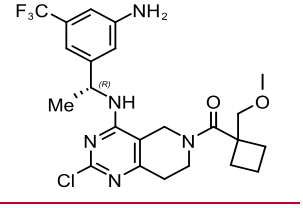
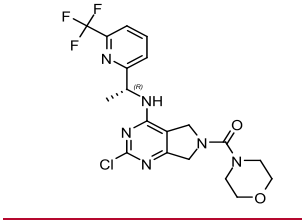
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Example 168.		Example 437.	
Example 169.		Example 438.	
Example 170.		Example 439.	

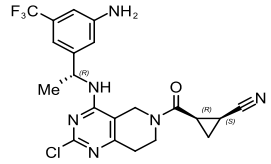
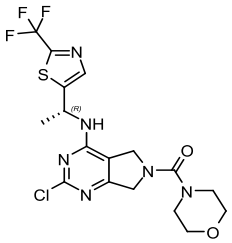
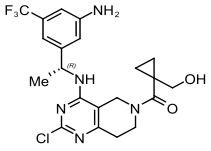
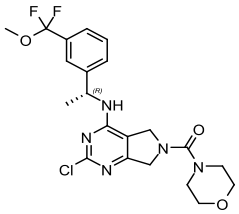
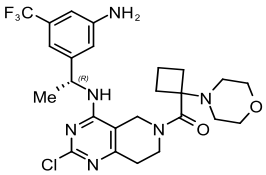
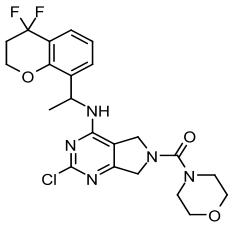
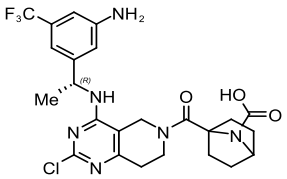
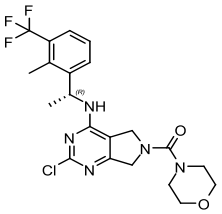
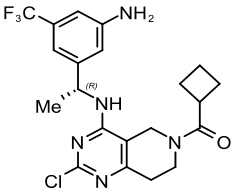
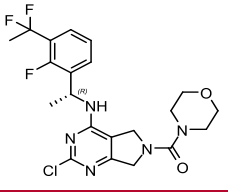
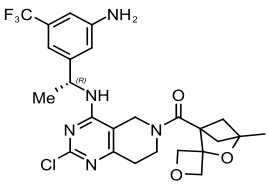
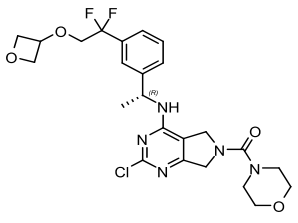
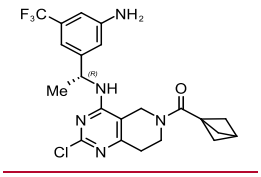
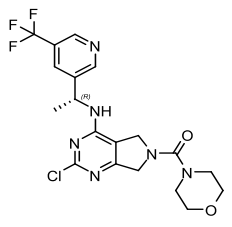
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Example 175.		Example 444.	
Example 176.		Example 445.	

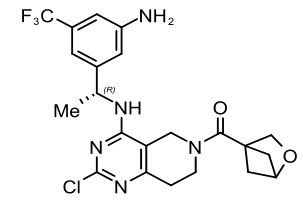
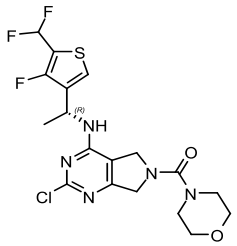
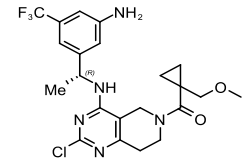
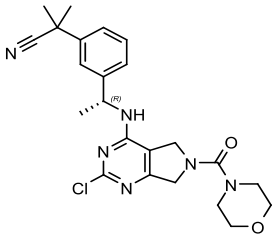
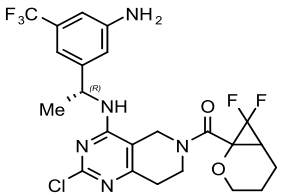
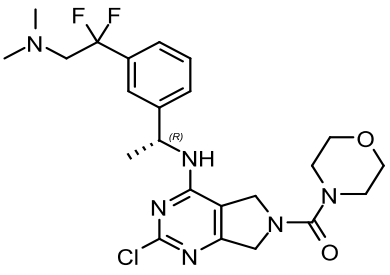
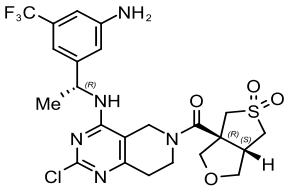
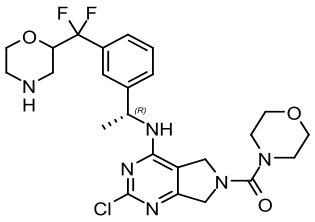
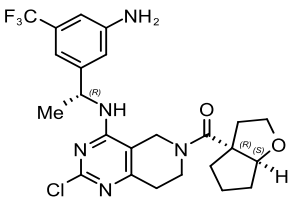
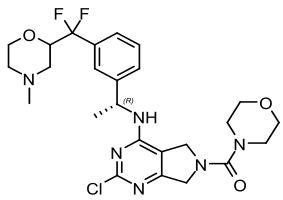
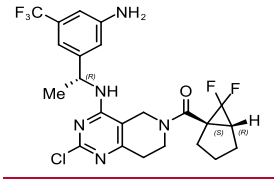
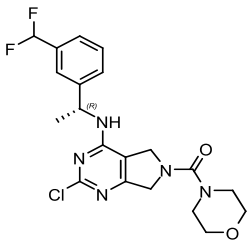
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Example 181.		Example 450.	
Example 182.		Example 451.	
Example 183.		Example 452.	

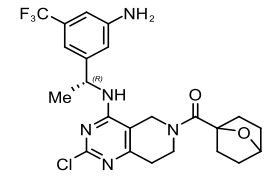
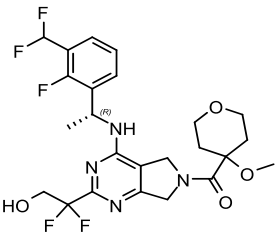
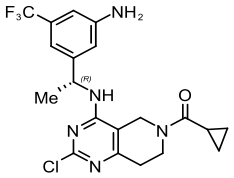
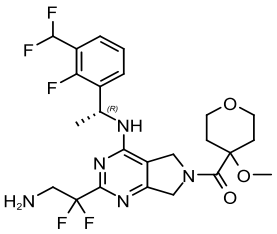
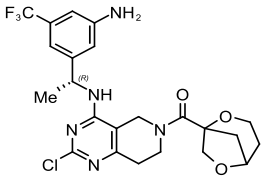
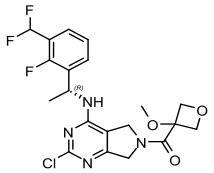
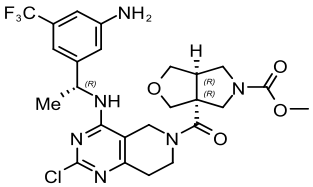
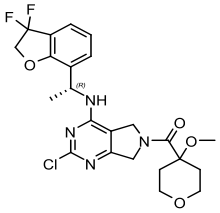
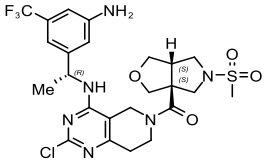
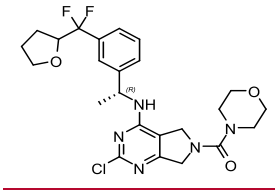
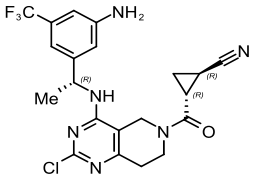
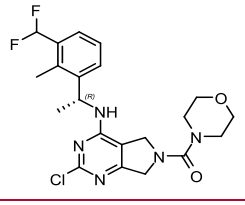
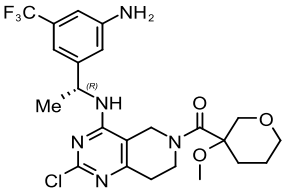
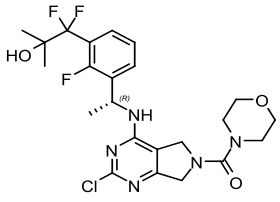
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Example 188.		Example 457.	
Example 189.		Example 458.	
Example 190.		Example 459.	

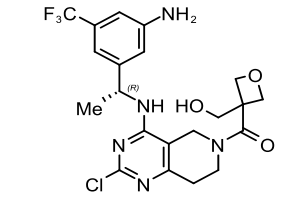
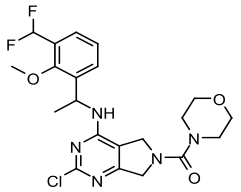
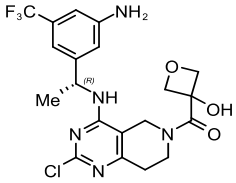
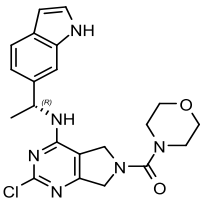
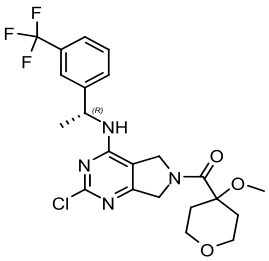
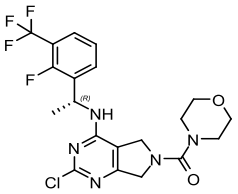
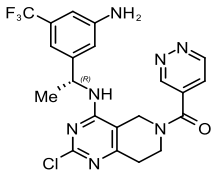
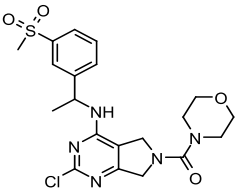
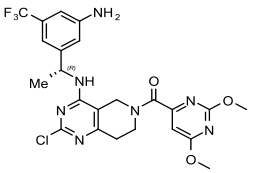
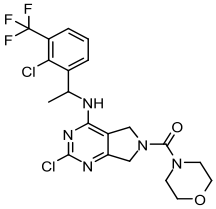
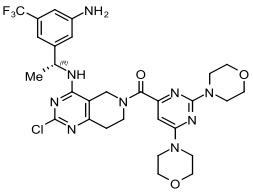
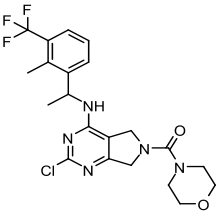
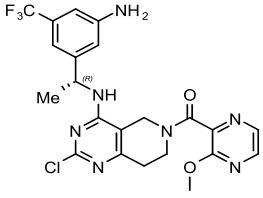
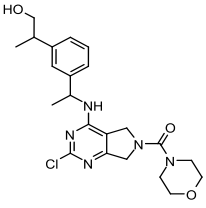
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Example 195.		Example 464.	
Example 196.		Example 465.	
Example 197.		Example 466.	

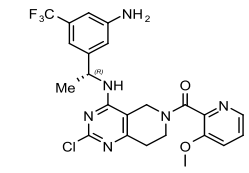
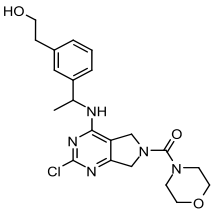
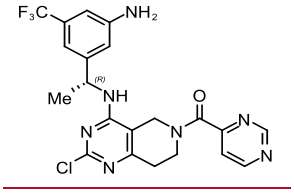
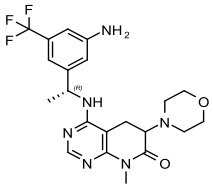
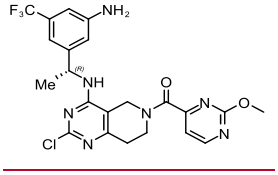
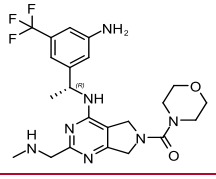
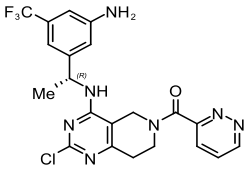
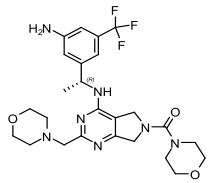
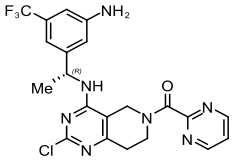
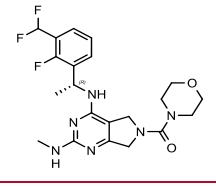
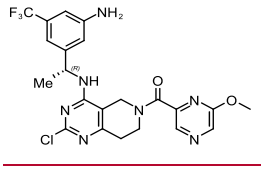
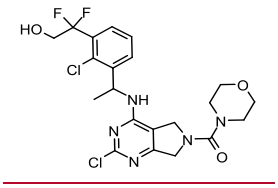
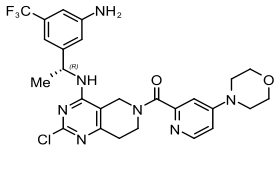
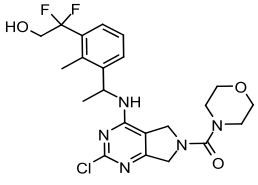
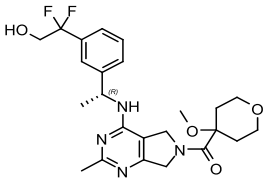
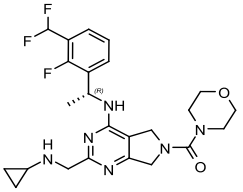
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Example 202.		Example 471.	
Example 203.		Example 472.	
Example 204.		Example 473.	

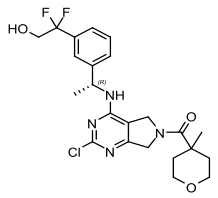
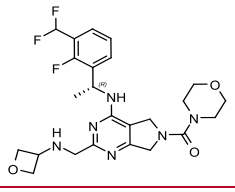
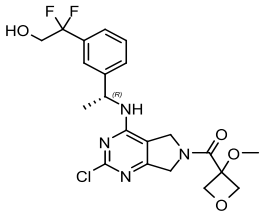
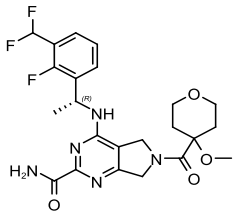
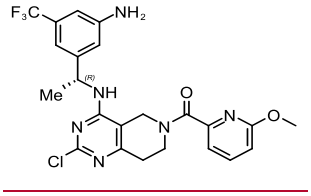
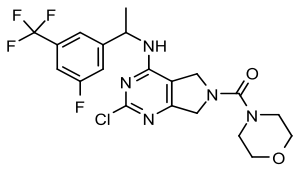
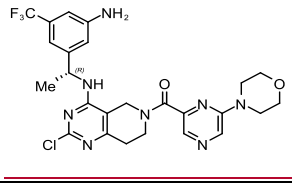
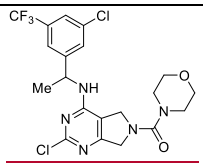
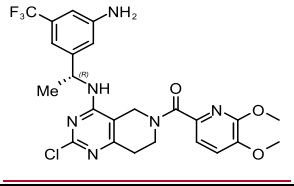
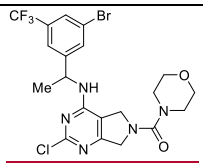
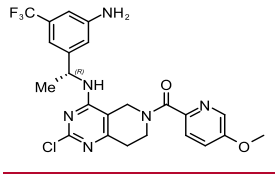
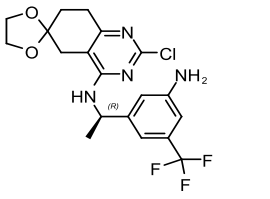
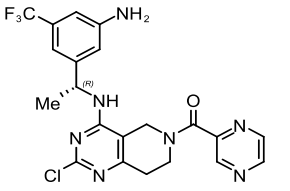
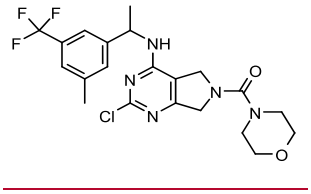
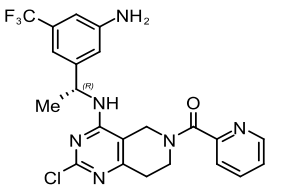
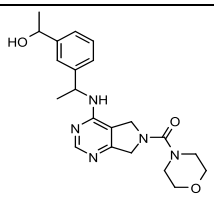
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Example 209.		Example 478.	
Example 210.		Example 479.	
Example 211.		Example 480.	

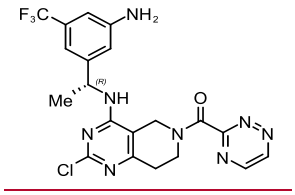
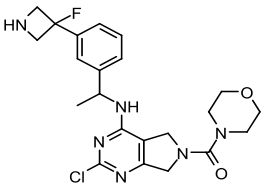
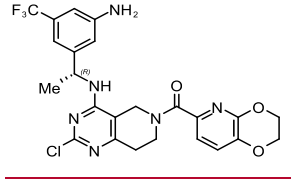
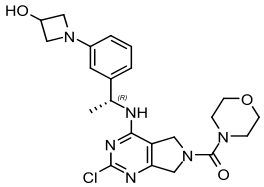
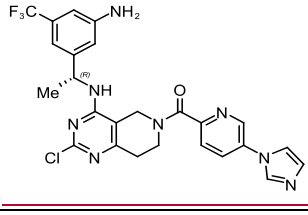
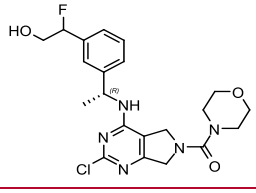
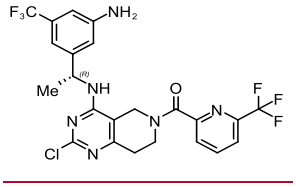
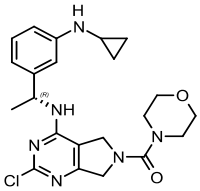
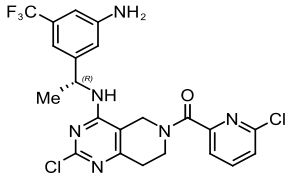
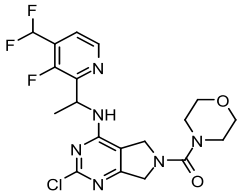
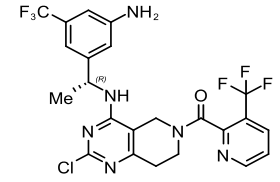
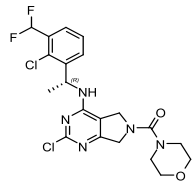
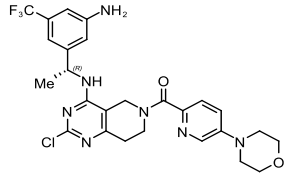
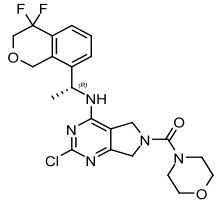
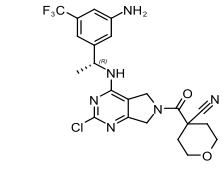
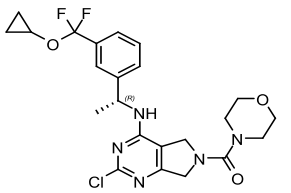
Example 212.		Example 481.	
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Example 215.		Example 484.	
Example 216.		Example 485.	
Example 217.		Example 486.	

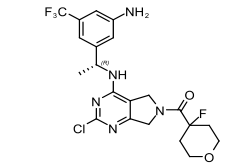
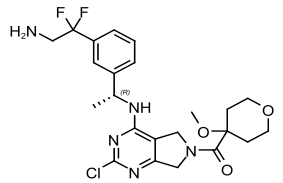
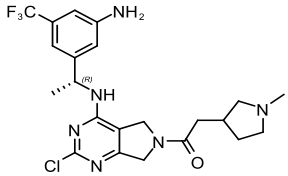
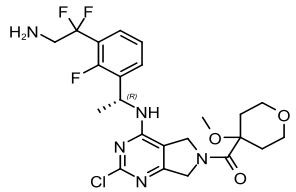
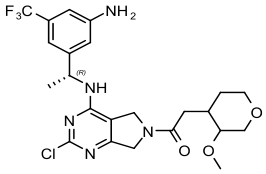
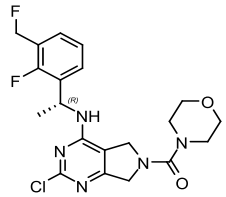
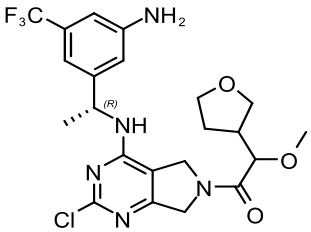
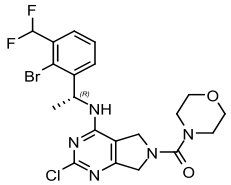
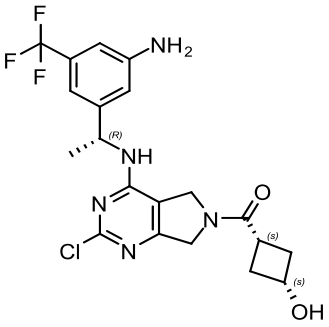
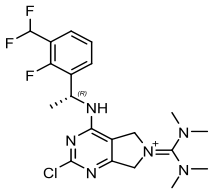
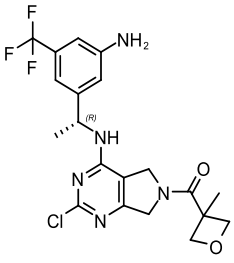
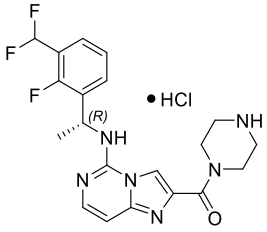
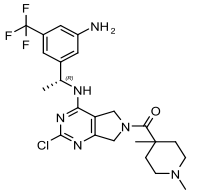
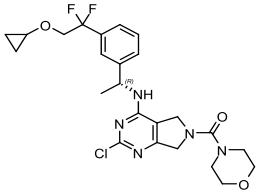
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Example 222.		Example 491.	
Example 223.		Example 492.	
Example 224.		Example 493.	

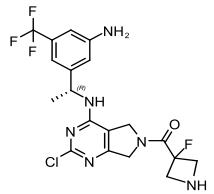
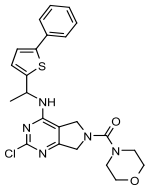
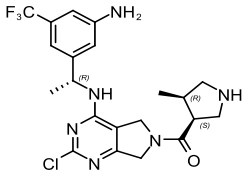
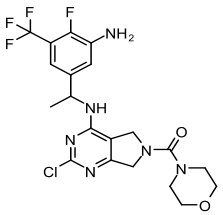
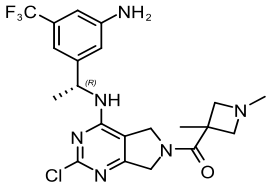
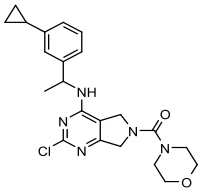
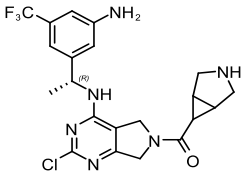
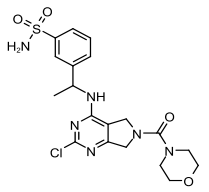
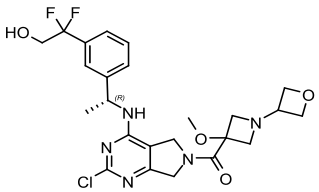
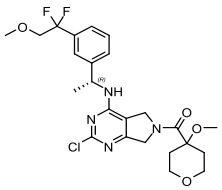
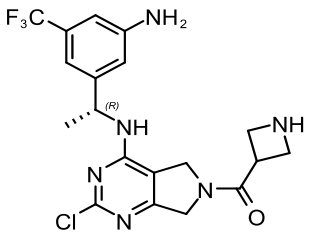
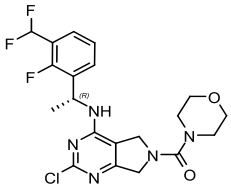
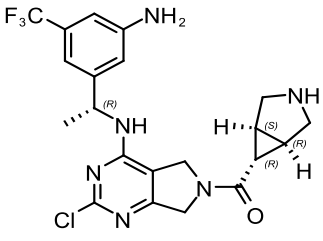
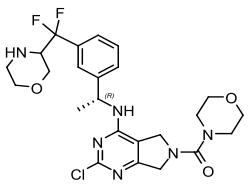
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Example 230.		Example 499.	
Example 231.		Example 500.	

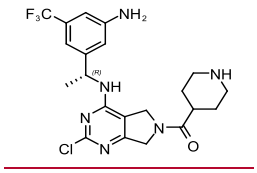
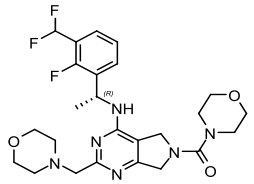
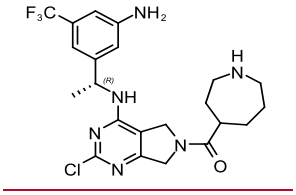
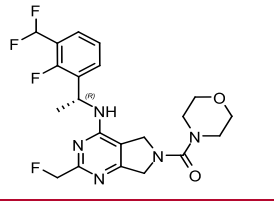
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Example 235.		Example 504.	
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Example 237.		Example 506.	
Example 238.		Example 507.	
Example 239.		Example 508.	

Example 240.		Example 509.	
Example 241.		Example 510.	
Example 242.		Example 511.	
Example 243.		Example 512.	
Example 244.		Example 513.	
Example 245.		Example 514.	
Example 246.		Example 515.	
Example 247.		Example 516.	

Example 248.		Example 517.	
Example 249.		Example 518.	
Example 250.		Example 519.	
Example 251.		Example 520.	
Example 252.		Example 521.	
Example 253.		Example 522.	
Example 254.		Example 523.	
Example 255.		Example 524.	

Example 256.		Example 525.	
Example 257.		Example 526.	
Example 258.		Example 527.	
Example 259.		Example 528.	
Example 260.		Example 529.	
Example 261.		Example 530.	
Example 262.		Example 531.	

Example 263.		Example 532.	
Example 264.		Example 533.	
Example 265.		Example 534.	
Example 266.		Example 535.	
Example 267.		Example 536.	
Example 268.		Example 537.	
Example 269.		Example 538.	

Example 270.		**Example 539.**	
Example 271.		**Example 540.**	

~~23~~14. A pharmaceutical composition comprising a compound of any one of claims 1-~~22~~13, or a pharmaceutically acceptable salt, solvate, stereoisomer, ~~hydrate,~~ or tautomer~~, or isomer~~ thereof, and a pharmaceutically acceptable carrier.

~~24. Use of a compound of any one of claims 1-22, or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or isomer thereof, in the manufacture of a medicament for inhibiting SOS1 in a subject.~~

~~25. Use of a compound of any one of claims 1-22, or a pharmaceutically acceptable salt, solvate, hydate, 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.~~

~~26. Use of a compound of any one of claims 1-22, 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.~~

~~27~~15. Use of a compound of any one of claims 1-~~22~~13, or a pharmaceutically acceptable salt, solvate, stereoisomer, ~~hydrate,~~or tautomer~~, or isomer~~ thereof, in the manufacture of a medicament for treating or preventing cancer in a subject in need thereof.

~~28~~16. A compound of any one of claims 1-~~22~~13, or a pharmaceutically acceptable salt, solvate, stereoisomer, ~~hydrate,~~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.

~~29~~17. The use of claim 15~~26 or 27~~, or the compound for use of claim ~~28~~16, 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.

~~30~~18. The use or compound for use of claim ~~29~~17, wherein the disease is a RASopathy.

~~31~~19. The use or compound for use of claim ~~30~~18, 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.